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Docket Number: **BURN1110**

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53 (c).

INVENTOR(s)/APPLICANT(s)

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TITLE OF INVENTION (280 characters max)

MOLECULE, FUNCTIONAL MOLECULE AND PROCESS FOR MANUFACTURING THEREOF, COMPOSITION, PHARMACEUTICAL, FOOD, BEVERAGE, MILK, TRANSGENIC MAMMAL, PROCESS FOR INHIBITING GROWTH OF BACTERIA, PROCESS FOR TREATING AND PREVENTING GASTRIC ULCERS, AND METHOD FOR TREATING GASTRIC CANCER

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ENCLOSED APPLICATION PARTS (*check all that apply*)

X	Specification - *Number of Pages:*	56		X	Other (*specify*): Cover Sheet, Claim Sheets, Abstract	1, 10, 1 page(s), respectively
X	Drawings, Appendix 1, Appendix A, Sequence Listing *Number of Pages:*	5, 57, 13, 3				

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (*check one*)

X	A check is enclosed to cover the filing fees: Check No. 549829 in the amount of $80.00			FILING FEE AMOUNT:
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	The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.			
	No			
X	Yes, the name of the U.S. Government agency and the Government contract number are: National Cancer Institute Grant Nos. CA 71932 and CA 33000			

Respectfully submitted,

SIGNATURE: Lisa Haile DATE: February 20, 2004

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PROVISIONAL

APPLICATION

for

UNITED STATES LETTERS PATENT

on

MOLECULE, FUNCTIONAL MOLECULE AND PROCESS FOR MANUFACTURING THEREOF, COMPOSITION, PHARMACEUTICAL, FOOD, BEVERAGE, MILK, TRANSGENIC MAMMAL, PROCESS FOR INHIBITING GROWTH OF BACTERIA, PROCESS FOR TREATING AND PREVENTING GASTRIC ULCERS, AND METHOD FOR TREATING GASTRIC CANCER

by

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Sheets of Drawings: Five (5)
Appendices:
Appendix 1 with Four (4) Figures
Appenidix A
Sequence Listing
Docket No.: BURN1110

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MOLECULE, FUNCTIONAL MOLECULE AND PROCESS FOR MANUFACTURING THEREOF, COMPOSITION, PHARMACEUTICAL, FOOD, BEVERAGE, MILK, TRANSGENIC MAMMAL, PROCESS FOR INHIBITING GROWTH OF BACTERIA, PROCESS FOR TREATING AND PREVENTING GASTRIC ULCERS, AND METHOD FOR TREATING GASTRIC CANCER

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to substances which can be used suitably for any one of remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, remedies for gastritis, and drugs for alleviating chronic gastritis; processes for producing the substances; processes for treating gastric ulcer by using the substances; and transgenic mammals capable of producing the substances.

Description of the Related Art

Helicobacter pylori is a microaerobic, gram negative and rod-shaped bacterium (bacillus) which lives on the lining of the stomach of about half the people on earth. It is considered to be a major cause of gastritis, chronic gastritis, gastric ulcer and duodenal ulcer. A relationship between *Helicobacter pylori* and diseases such as gastric cancer has also been reported. Development of a remedy for diseases caused by *Helicobacter pylori* is an important theme for maintaining health and well-being.

Antibiotics such as penicillin, tetracycline, cephalosporin and neuroquinone are known to be anti-*Helicobacter pylori* agents. However, although they exhibit antibacterial action against *Helicobacter pylori*, single administration of these agents is

not sufficient to kill the bacteria. Recently, triple therapy has mainly been conducted using these antibiotics together with a bismuth agent and proton pump inhibitor. In addition, an anti-*Helicobacter pylori* agent containing benzohydroxamic acid has been proposed (Japanese Patent Application Laid-Open (JP-A) No. 11-189529). It is, however, inferior from the point of view of safety, because side effects such as diarrhea and vomiting can result.

An anti-*Helicobacter pylori* agent containing steryl glucopyranoside extracted from plants has also been proposed (JP-A No. 2003-73278). Further, an anti-*Helicobacter pylori* agent containing a component extracted from crude drugs such as Coptidis Rhizoma and a hydrogen carbonate of an alkali metal has been proposed (JP-A No. 2002-370995). However, these agents have side effects because they are not produced in the human living body and moreover, their antibacterial effects against *Helicobacter pylori* are insufficient. None of the above-described proposals includes disclosure about deterioration in the motility and abnormal morphology of *Helicobacter pylori*.

Substances having sufficient antibacterial effects, being free from side effects and having excellent safety, and their application technique have not yet been proposed and there is therefore a demand for the development of such substances and techniques.

SUMMARY OF THE INVENTION

Accordingly, an object of the present invention is to provide molecules, functional molecules, compositions, pharmaceuticals, foods, beverages, and milk which possess antibacterial activity, which includes inhibiting growth and motility and causing abnormal morphology, against *Helicobacter* genus bacteria, wherein the antibacterial activity against *Helicobacter* genus bacteria is selective and specific, thereby being free

of side effects and possessing extremely high safety; and transgenic mammals. The present invention also provides processes for efficient manufacturing of the functional molecules; and processes for treating gastric cancer or gastric ulcers and preventing gastric ulcers which include administering the functional molecules thereby being free of side effects and possessing extremely high safety.

In view of the problems stated above, the inventors of the present invention have conducted intensive studies and obtained the following new findings. As shown in FIG. 1, when patients infected with *Helicobacter pylori* are examined, it is observed that the microbes are solely associated with surface mucous cell-type mucin secreted from surface mucous cells which constitute the surface portion of stomach lining, but they do not colonize the gland mucous cells which are present in the deeper portions of the stomach lining. It is also found that gland mucous cell-type mucin, secreted from gland mucous cells, contains N-acetylglucosamine residues which are linked at its terminals by the α1,4-glycosidic bonds (herein after may be referred to as "GlcNAcα (residue)"), and that the terminal GlcNAcα residues inhibit the synthesis of cholesteryl-α-D-glucopyranoside (CGL), which is contained in the cell wall of *Helicobacter pylori*, resulting possibly in inhibiting the growth properties of *Helicobacter pylori*, additionally inhibiting the motility thereof, and causing abnormal morphologies thereof. In FIG. 1, "GlcNAcα (+)" means that mucin containing a GlcNAcα residue is present, and "GlcNAcα (-)" means that mucin with no GlcNAcα residue is present. It is derived from the fact that α1,4-GlcNAc residues can be stained by PCS staining (in brown), whereas GOCTS stains superficial mucins (in blue).

The present invention is based on the findings described above and includes means for solving the problems mentioned above. It includes:

<1> A molecule, comprising a plurality of monomer units, wherein at least one of the monomer units is an N-acetylglucosamine residue. According to <1>, the molecule suppresses or inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<2> A molecule according to <1>, wherein the molecule is a sugar chain.

<3> A molecule according to <1>, wherein the N-acetylglucosamine residue exists at a terminal of the molecule.

<4> A molecule according to <1>, wherein the N-acetylglucosamine residue is an α1,4-N-acetylglucosamine residue. According to the molecule of <4>, the α1,4-N-acetylglucosamine residue suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<5> A molecule according to <1>, further comprising a galactose residue, wherein the galactose residue exists adjacent to the N-acetylglucosamine residue.

<6> A molecule according to <1>, which is at least one of linear and branched.

<7> A composition, comprising a molecule according to <1>.

<8> A composition according to <7>, to be used for one of a pharmaceutical and edible composition such as food and beverage.

<9> A functional molecule, comprising a molecule according to <1>. The functional molecule according to <9> suppresses and inhibits the synthesis of

cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<10> A functional molecule according to <9>, comprising a main chain and a side chain, wherein the side chain is the molecule according to Claim 1.

<11> A functional molecule according to <10>, wherein the main chain is a polypeptide.

<12> A functional molecule according to <9>, wherein the molecule according to <1> exists in the cluster form relative to the main chain. According to the functional molecule of <12>, since the molecule exists in the cluster form relative to the main chain, it suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<13> A functional molecule according to <9>, capable of suppressing or inhibiting the synthesis of cholesteryl-α-D-glucopyranoside (CGL). Since the functional molecule of <13> is capable of suppressing or inhibiting the synthesis of cholesteryl-α-D-glucopyranoside, it in turn suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<14> A functional molecule according to <11>, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

<15> A functional molecule according to <10>, wherein a ratio of the number of the side chain to the main chain is 10 or more.

<16> A functional molecule according to <9>, to be used for at least one of a remedy for gastric ulcer, a remedy for duodenal ulcer, an anti-*H. pylori* agent, a remedy for gastritis, and a drug for alleviating chronic gastritis.

<17> A functional molecule according to <9>, to be used for an edible composition such as food or beverage.

<18> A composition, comprising a functional molecule according to <9>. Since the composition of <18> comprises the functional molecule, it suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<19> A pharmaceutical, comprising a functional molecule according to <9>. In the pharmaceutical of <19>, the functional molecule suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, by administering the pharmaceutical, it suppresses or inhibits the motility of bacteria existing in a living organism and requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<20> A pharmaceutical according to <19>, which is sprayed or coated to the mucous layer of at least one of the stomach and intestine.

<21> A pharmaceutical according to <19> to be used after impregnated or incorporated in at least one of a film and a sheet.

<22> A pharmaceutical according to <21>, wherein the at least one of a film and sheet is applied to the mucous layer of at least one of the stomach and intestine.

<23> A pharmaceutical according to <19>, comprising at least one of a cholesterol degradative enzyme and a glucose degradative enzyme. In the pharmaceutical of <23>, the cholesterol degradative enzyme degrades cholesterol and the glucose degradative enzyme degrades glucose. Accordingly, it suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, by administering the pharmaceutical, it suppresses or inhibits the motility of bacteria existing in a living organism and requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<24> An edible composition, which comprises a functional molecule according to <9>. In the edible composition of <24>, the functional molecule suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, by taking in the edible composition, it suppresses or inhibits the motility of bacteria existing in a living organism and requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<25> A process for producing a functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising the step of:

contacting

α1,4-N-acetylglucosaminyl transferase (α4GnT),

at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a polypeptide having at least one O-glycosylated region, thereby producing a functional molecule having at least one α1,4-N-acetylglucosamine residue. According to the process for producing a functional molecule of <25>, the α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and the polypeptide having at least one O-glycosylated region contact, thereby producing the functional molecule.

<26> A process for producing a functional molecule according to <25>, wherein the polypeptide is a soluble polypeptide.

<27> A process for producing a functional molecule according to <25>, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

<28> A process for producing a functional molecule according to <25>, wherein the polypeptide is mucin secreted into milk of mammals.

<29> A process for producing a functional molecule according to <25>, further comprising isolating the functional molecule having at least one α1,4-N-acetylglucosamine residue after production thereof.

<30> A functional molecule obtained by a process for producing a functional molecule according to <25>. The functional molecule according to <30> suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, by administering the pharmaceutical, it suppresses or inhibits the motility of

bacteria existing in a living organism and requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<31> A process for producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising:

expressing, in a eukaryotic cell,

a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT),

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

<32> A process for producing a functional molecule according to <31>, wherein at least one of the first, second and third polynucleotides is an exogenous polynucleotide introduced into the eukaryotic cell. According to the process for producing a functional molecule of <31>, by expressing, an α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and a polypeptide having at least one O-glycosylated region are expressed. Subsequently, the α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and polypeptide having at least one O-glycosylated region at least contact with each other thereby producing a functional molecule.

<33> A process for producing a functional molecule according to <31>, wherein the polypeptide is a soluble polypeptide.

<34> A process for producing a functional molecule according to <31>, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

<35> A process for producing a functional molecule according to <31>, wherein the eukaryotic cell is a cell of a mammal.

<36> A process for producing a functional molecule according to <31>, further comprising:

contacting

the α4GnT-I,

at least one of the C2GnT-I and the C1-β3GnT, and

the polypeptide having at least one O-glycosylated region, after expressing,

thereby producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue.

<37> A process for producing a functional molecule according to <36>, further comprising isolating the recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue after production thereof.

<38> A functional molecule obtained by a process for producing a functional molecule according to <31>. The functional molecule according to <38> suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<39> A transgenic mammal other than humans and capable of secreting milk, wherein its genome comprises:

a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT);

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT); and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region. In the transgenic mammal according to <39>, an α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and a polypeptide having at least one O-glycosylated region are expressed. Subsequently, the α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and polypeptide having at least one O-glycosylated region at least contact with each other thereby producing a functional molecule.

<40> A transgenic mammal according to <39>, wherein at least one of the first polynucleotide, second polynucleotide and third polynucleotide is an exogenous polynucleotide.

<41> A transgenic mammal according to <39>, wherein at least one of the first polynucleotide, second polynucleotide and third polynucleotide is introduced into the genome so as to be linked operatively with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

<42> A transgenic mammal according to <39>, wherein the third polynucleotide is introduced into the genome so as to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing the polypeptide having at least one O-glycosylated region to be secreted in the milk.

<43> A transgenic mammal according to <41>, wherein the 5' regulatory sequence has a promoter.

<44> A transgenic mammal according to <43>, wherein the promoter is at least one promoter selected from whey acidic protein (WAP) promoter, α-casein promoter, β-casein promoter, γ-casein promoter, α-lactalbumin promoter and β-lactoglobulin promoter.

<45> A transgenic mammal according to <39>, wherein the first, second and third polynucleotides form one nucleic acid molecule and the nucleic acid molecule is introduced into the genome so as to be operatively linked with either one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating the mammary gland.

<46> A transgenic mammal according to <39>, wherein the mammal is one of mouse, rat, rabbit, horse, pig, sheep, goat and cow.

<47> A process for producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising:

introducing a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT) into an embryo of a mammal other than humans;

transplanting the embryo to a recipient female mammal;

causing the recipient female mammal to produce offspring thereof; and

causing female offspring, among offspring produced, to produce milk.

According to the process for producing a recombinant functional molecule of <47>, in the body of the offspring, an α1,4-N-acetylglucosaminyl transferase (α4GnT) is

expressed. The α1,4-N-acetylglucosaminyl transferase (α4GnT) at least contacts with a polypeptide which is present in the body of the offspring thereby producing a functional molecule.

<48> A process for producing a functional molecule according to <47>, wherein the first polynucleotide is introduced into the embryo so as to be operatively linked with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

<49> A process for producing a functional molecule according to <47>, further comprising introducing, into the embryo,

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

<50> A process for producing a functional molecule according to <47>, wherein at least one of the second polynucleotide and third polynucleotide is introduced into the embryo so as to be operatively linked with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

<51> A process for producing a functional molecule according to <49>, wherein the third polynucleotide is introduced into the embryo so as to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing secretion of a polypeptide having at least one O-glycosylated region into the milk.

<52> A process for producing a functional molecule according to <47>, further comprising milking after causing the female offspring to produce milk.

<53> A process for producing a functional molecule according to <47>, further comprising isolating the recombinant functional molecule from the milk.

<54> Milk obtained by a process for producing a functional molecule according to <47>. The milk according to <54> suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<55> A functional molecule obtained by a process for producing a functional molecule according to <47>. The functional molecule according to <55> suppresses and inhibits the synthesis of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<56> A process for inhibiting bacterial growth, comprising:

contacting bacteria expressing cholesteryl-α-D-glucopyranoside (CGL) with a functional molecule having at least one α1,4-N-acetylglucosamine residue so as to suppress or inhibit at least one of growth of the bacteria and formation of cell walls of the bacteria. According to the process for inhibiting bacterial growth of <58>, the functional molecule suppresses and inhibits the expression (synthesis) of cholesteryl-α-D-glucopyranoside and in turn, suppresses and inhibits at least one of the growth of bacteria requiring the cholesteryl-α-D-glucopyranoside and formation of cell walls of the bacteria. Moreover, it suppresses or inhibits the motility of bacteria requiring the cholesteryl-α-D-glucopyranoside, and causes abnormal morphologies of the bacteria.

<57> A process for inhibiting bacterial growth according to <56>, wherein the functional molecule having an α1,4-N-acetylglucosamine residue can suppress or inhibit the activity of UDP-Glc:sterol glycosyltransferase.

<58> A process for inhibiting bacterial growth according to <56>, wherein the bacteria are *Helicobacter* genus bacteria.

<59> A process for inhibiting bacterial growth according to <58>, wherein the *Helicobacter* genus bacteria are *Helicobacter pylori*.

<60> A process for inhibiting bacterial growth according to <56>, wherein the functional molecule having at least one α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

<61> A process for treating gastric ulcer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue so as to alleviate signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* genus bacteria. In the process for treating gastric ulcer according to <61>, the functional molecule suppresses and inhibits the expression (synthesis) of cholesteryl-α-D-glucopyranoside and in turn, alleviates signs or symptoms of gastric ulcer induced by the infection with the *Helicobacter* genus bacteria, which requires cholesteryl-α-D-glucopyranoside.

<62> A process for treating gastric ulcer according to <61>, wherein the *Helicobacter* genus bacteria are *Helicobacter pylori*.

<63> A process for treating gastric ulcer according to <61>, wherein the subject is a mammal.

<64> A process for treating gastric ulcer according to <61>, wherein the mammal is one of mouse, rat, rabbit, horse, pig, sheep, goat and cow.

<65> A process for treating gastric ulcer according to <61>, wherein the subject is human being.

<66> A process for treating gastric ulcer according to <61>, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

<67> A process for treating gastric ulcer according to <61>, wherein the administration is oral administration.

<68> A process for treating gastric ulcer according to <61>, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

<69> A process for treating gastric ulcer according to <61>, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

<70> A process for treating gastric ulcer according to <61>, wherein the functional molecule is administered by using the milk according to <54>.

<71> A process for preventing gastric ulcer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue so as to prevent signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* genus bacteria. In the process for preventing gastric ulcer according to <71>, the functional molecule suppresses and inhibits the expression (synthesis) of cholesteryl-α-D-glucopyranoside and in turn, prevents signs or symptoms of gastric ulcer induced by the infection with the *Helicobacter* genus bacteria, which requires cholesteryl-α-D-glucopyranoside.

<72> A process for preventing gastric ulcer according to <71>, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

<73> A process for preventing gastric ulcer according to <71>, wherein the administration is oral administration.

<74> A process for preventing gastric ulcer according to <71>, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

<75> A process for preventing gastric ulcer according to <71>, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

<76> A process for treating gastric ulcer according to <71>, wherein the administration is performed using the milk according to <54>.

<77> A process for treating gastric cancer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue to alleviate signs or symptoms of gastric cancer induced by the infection of a subject with *Helicobacter* genus bacteria. In the process for treating gastric cancer according to <77>, the functional molecule suppresses and inhibits the expression (synthesis) of cholesteryl-α-D-glucopyranoside and in turn, alleviates signs or symptoms of gastric cancer induced by the infection with the *Helicobacter* genus bacteria, which requires cholesteryl-α-D-glucopyranoside.

<78> A process for treating gastric cancer according to <77>, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

<79> A process for treating gastric cancer according to <77>, wherein the administration is oral administration.

<80> A process for treating gastric cancer according to <77>, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

<81> A process for treating gastric cancer according to <77>, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

<82> A process for treating gastric cancer according to <77>, wherein the administration is performed by using the milk according to <54>.

Further aspects of the present invention are disclosed in Appendix 1, which is attached hereto, and in Appendix A, which is attached to Appendix 1.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic cross-sectional view of a general gastric wall of humans, showing that α1,4-GlcNAc residues are stained by PCS staining (in brown), whereas GOCTS stains superficial mucins (in blue).

FIG. 2A is one example of a graph showing the growth of *Helicobacter pylori*.

FIG. 2B is one example of a time-lapse photograph of typical *Helicobacter pylori* on a medium taken at an interval of 1 second.

FIG. 2C is one example of an SEM photograph of *Helicobacter pylori* after incubation.

FIG. 3 is one example of mass spectra of a sample of *Helicobacter pylori* synthesized in vivo and that in vitro.

FIG. 4 is one example of analysis results of thin-film chromatography of a glycolipid portion extracted from *Helicobacter pylori* cultured in the presence or absence of cholesterol.

FIG. 5 is one example of micrographs of gastric adenocarcinoma cells (AGS cells) which stably express G1cNAc-CD43 and gastric adenocarcinoma cells (AGS cells) which stably express G1cNA-free CD43 when these gastric adenocarcinoma cells are cultured together with *Helicobacter pylori*.

DESCRIPTION OF THE PREFERED EMBODIMENTS

(Molecule) - The molecule of the present invention contains, as a portion thereof, an N-acetylglucosamine (which may hereinafter be called "GlcNAc") and optionally contains a molecule constituting unit selected properly as needed.

(GlcNAc residue) - The GlcNac residue is a residue of GlcNAc and it may be any one of chemically synthesized product, extract from natural products and that existing in the living body.

No particular limitation is imposed on the production process of the GlcNac and it can be produced by a process selected as needed from known processes. For example, it can be produced by hydrolyzing chitin in hydrochloric acid and then isolating the hydrolysate.

(Molecule constituting unit) - No particular limitation is imposed on the molecule constituting unit and it can be selected as needed according to its using purpose. Examples include sugar residues and resin units, of which sugar residues are preferred. They may be used either alone or in combination of two or more.

The sugar residues may be either monosaccharide residues or polysaccharide residues. Examples of the monosaccharide residues or monosaccharide residues

constituting polysaccharide residues include galactose, tetrose, erythrose, threose, pentose, ribose, arabinose, xylose, lyxose, hexose, arose, altrose, glucose, mannose, gulose, idose, talose, tetrulose, erythrulose, 2-pentylose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, 2-hepturose, sedoheptulose, quinovose, rhamnose, fucose, digitoxose, abequose, tyvelose, 2-deoxyribose, 2-deoxyglucose, glucosamine, mannosamine, galactosamine, fucosamine, quinovosamine, rhamnosamine, neuraminic acid, muramic acid, and nojirimycin residues. Of these, galactose residue is especially preferred as a sugar residue adjacent to the GlcNAc residue. The above-described sugar residues may be used either alone or in combination of two or more. They may have a substituent inserted therein or may be substituted further with another substituent.

Examples of the resin unit include L-lactide and D-lactide. Preferred are units constituting a biocompatible molecule.

No particular limitation is imposed on the molecule and it can be selected as needed depending on the using purpose. When the other unit is the sugar residue, the molecule is preferably an oligosaccharide chain.

No particular limitation is imposed on the position of the GlcNAc residue in the molecule of the present invention. It may exist either at the terminal position of the molecule or at a position other than the terminal position. Existence at the terminal position is preferred from the viewpoint of excellent antibacterial effects.

When the molecule is the above-described sugar chain, no particular limitation is imposed on the linkage of the GlcNAc residue. It may be either α-glycoside linkage or β-glycoside linkage. Of these, α1,4-glycoside linkage is especially preferred.

No particular limitation is imposed on an enzyme which combines the GlcNAc residue with the molecule through the α1,4-glycoside linkage and it can be selected as

needed, depending on the using purpose. For example, N-acetylglucosaminyl transferase (α4GnT) as described in JP-A No. 2001-46077 is especially preferred.

Although no particular limitation is imposed on the production process of the α4GnT, it can be produced, for example, by forming a DNA encoding the α4GnT in accordance with the process as described in JP-A No. 2001-46077, transfecting various cells with a vector having the DNA incorporated therein and causing expression of the α4GnT.

With regards to the α4GnT, it is possible to refer to, for example, the description of J. Nakayama et al., Proc. Natl. Acad. Sci. U.S.A. 96, 8991 (1999).

No particular limitation is imposed on the number of monomer units (GlcNAcα residues and molecule constituting units) in the molecule of the present invention and it can be selected as needed depending on the using purpose. For example, the number is preferably 2 or greater, more preferably from 2 to 30, especially preferably from 5 to 20.

When the number of monomer units is less than 2, the molecule will not possess antibacterial effect.

No particular limitation is imposed on the shape of the molecule of the invention and it may be either linear or branched.

The number of branches when the molecule is branched is not particularly limited and may be selected as needed depending on the using purpose. For example, it is preferably from 1 or more, more preferably from 5 or more.

In general, the larger the number of braches is, the higher the antibacterial effect becomes.

No particular limitation is imposed on the enzyme for branching the molecule and it can be selected as needed, depending on the using purpose. For example, core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) is especially preferred.

Although no particular limitation is imposed on the production process of the C2GnT-I, it can be produced by introducing a gene into a cell, preparing C2GnT-I by genetic modification, isolating and purifying from an organism, or the like.

With regards to the C2GnT-I, it is possible to refer to, for example, the description of M. F. A. Bierhuizen, M. Fukuda, Proc. Natl. Acad. Sci. U.S.A. 89, 9326 (1992).

No particular limitation is imposed on the enzyme for binding the sugar residue in the molecule and it can be selected as needed, depending on the using purpose. For example, core 1 elongation β1,3-N-acetylglucosaminyl transferase (C1-β3GnT) can be used.

With regards to the C1-β3GnT, it is possible to refer to, for example, the description of Yeh et al., Cell 105:957-969, 2001.

When the molecule of the present invention is a sugar chain containing a GlcNAcα residue, it is similar to a molecule possessed by gland mucous cell-type mucin secreted from gland mucous cells existing in the deep portion of the human stomach wall, or a molecule having a structure analogous thereto. It therefore has no side effects and is highly safe even when used as a pharmaceutical or an edible composition such as food or beverage. Use of it is therefore advantageous.

The molecule of the present invention can be employed in various fields. It can suitably be used for remedies for diseases caused by *Helicobacter pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, remedies for gastritis, or drug for alleviating chronic gastritis), particularly for the functional molecule and composition of the present invention which will be described below.

(Functional Molecule) - The functional molecule of the present invention comprises the above-described molecule of the present invention and optionally has another molecule selected as needed. The molecule of the present invention has already been described above.

The functional molecule of the present invention preferably has a main chain and a side chain, with that having the molecule of the present invention as the side chain being especially preferred. The molecule preferably exists in the cluster form relative to the main chain. The term "in the cluster form" as used herein means a state in which 10 or more molecules, which have been described above, are linked, at the terminals thereof, to one main chain.

There is no particular limitation imposed on a ratio of the number of the main chain to the number of the side chains and it can be selected as needed, depending on the using purpose. For example, when the main chain is a protein, the ratio is limited by the types of the amino acid residues which constitute the protein.

In general, the more the number of side chains relative to one main chain is, the higher the antibacterial effect becomes.

The functional molecule of the present invention capable of suppressing or inhibiting the synthesis of the CGL is especially preferred. By suppressing or inhibiting the synthesis of the CGL, growth of bacteria requiring the CGL can be suppressed or inhibited.

Examples of the bacteria requiring the CGL include *Helicobacter* genus bacteria. The *Helicobacter* genus bacteria include *Helicobacter pylori*.

In human, the functional molecule of the present invention possesses antibacterial activity selectively and specifically against *Helicobacter* genus bacteria and therefore it does not damage the bacterial layer in the intestine. Additionally,

when the functional molecule of the present invention includes a GlcNAcα residue, it is identical with gland mucous cell-type mucin secreted from gland mucous cells present in the deeper portion of human gastric wall or other functional molecules having structures similar to that of the mucin. Hence, the functional molecule of the present invention may be used as pharmaceutical, food, or beverage without side effects, which makes it extremely safe and therefore advantageous.

The *Helicobacter* genus bacteria contain, in the cell walls thereof, α-cholesteryl glucoside (which will hereinafter be called "α-CGs"). Examples of the main components of the α-CGs include CGL, cholesteryl-6-O-tetradecanoyl-α-D-glucopyranoside (which will hereinafter be called "CAG") and cholesteryl-6-O-phosphatidyl-α-D-glucopyranoside (which will hereinafter be called "CPG"). *Helicobacter* genus bacteria are one type of bacteria needing, for their survival, synthesis of CGL.

(Other molecules) - There is no particular limitation imposed on Other molecules and it can be selected as needed, depending on the using purpose. Examples include the above-described main chain, more specifically, sugar chains, polypeptides, lipids, glycolipids, sugar proteins, nucleotides, and resins such as polylactic acid. They may be used either alone or in combination of two or more. Of these, the polypeptides are preferred

No particular limitation is imposed on the polypeptides and they can be selected as needed, depending on the using purpose. Preferred examples include CD43, CD34 and Muc-6.

No particular limitation is imposed on the amino acid, in the polypeptide, which will bind to the molecule. Examples include phenylalanine (Phe), leucine (Leu), isoleucine (Ile), methionine (Met), valine (Val), serine (Ser), proline (Pro), threonine

(Thr), alanine (Ala), tyrosine (Tyr), histidine (His), glutamine (Gln), asparagine (Asn), lysine (Lys), aspartic acid (Asp), glutamic acid (Glu), cysteine (Cys), tryptophan (Trp), arginine (Arg) and glycine (Gly), of which serine (Ser) and threonine (Thr) are especially preferred.

(Production Process of Functional Molecule) - The functional molecule of the present invention can be produced by any one of the first to three aspects which will be described below.

These three aspects of the production processes of the functional molecule can be employed preferably as a production process of the functional molecule of the present invention. The milk of the present invention will be revealed through the description of the functional molecule of the present invention.

The first aspect of the production process is a production process of a functional molecule having at least one α1,4-N-acetylglucosamine residue, which comprises bringing α1,4-N-acetylglucosaminyl transferase (α4GnT), at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation beta-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and a polypeptide having at least one O-glycosylated region into contact with each other.

The second aspect of the production process is a production process of a recombinant type functional molecule having at least one α1,4-N-acetylglucosamine residue, which comprises at least a step of expressing, in eukaryotic cells, a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT), a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β1,3-N-acetylglucosaminyl transferase (C1-β3GnT) and a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

The third aspect of the production process is a production process of a recombinant type functional molecule having at least one α1,4-N-acetylglucosamine residue, which comprises introducing a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT) into an embryo of a mammal other than humans, transplanting the resulting embryo to a recipient female mammal, causing the female mammal to produce offspring thereof, and causing a female offspring, among offspring produced, to produce milk.

The α4GnT, the C2GnT-I and the C1-β3GnT have already been described above.

No particular limitation is imposed on the polypeptide insofar as it has at least one O-glycosylated region. Soluble polypeptides are preferred and examples include CD43, CD34, Muc-6, and mucin secreted in the milk of mammals.

In the above-described first aspect, it is preferred to contact the GlcNAc and sugar, in addition to the α4GnT, at least either one of the C2GnT-I and the C1-β3GnT and the polypeptide having at least one O-glycosylated region, with each other.

In the above-described second aspect, the functional molecule can be produced by contacting the α4GnT, at least either one of the C2GnT-I and the C1-β3GnT and the polypeptide having at least one O-glycosylated region with each other after the expression step. Further contacting with the GlcNAc and sugar is preferred.

No particular limitation is imposed on the eukaryotic cell and it can be selected as needed, depending on the using purpose. For example, cells of mammals are preferred.

Preferred examples of the cells of mammals include ovarian cells of Chinese hamsters (CHO cells).

In the second aspect of the production process, each of the first to third polypeptides may be either exogenous or endogenous.

The term "endogenous" as used herein means that when it is used concerning polynucleotide, the polynucleotide is found in specific cells or cells of organisms under natural conditions, while the term "exogenous" means that when it is used concerning polynucleotide, the polynucleotide is not found in specific cells or cells of organisms under natural conditions.

When the eukaryotic cells are mammary gland cells, the functional molecule can be produced by supplying the α4GnT as an exogenous one, because they can express C2GnT-I and the polypeptide having at least one O-glycosylated region. When the eukaryotic cells express the C2GnT-I, the functional molecule can be produced by supplying the α4GnT and the polypeptide having at least one O-glycosylated region as exogenous ones.

One example of the second aspect of the production process will next be described.

By amplifying a DNA fragment (a portion corresponding to the 20th to 254th amino acids of the amino acid sequence of SEQ. ID. No. 1) including the whole extracellular domain of the CD43 by the PCR method and subcloning the amplified DNA fragment into pSecTag2 (product of Invitrogen), Igκ leader peptide, myc epitope following it and a vector (pSecTag2-sCD43) encoding $(His)_6$ are produced.

Then, four vectors having, incorporated in the pSecTag2-sCD43,(1) a polynucleotide (cDNA) encoding C2GnT-I, (2) a polynucleotide (cDNA) encoding α4GnT, (3) a polynucleotide (cDNA) encoding soluble CD43, and (4) a polynucleotide (cDNA) encoding a polyoma·virus large T antigen, respectively are transfected into the CHO·Lec2 cells which have been cultured in advance, by using LipofectAmine (trade

mark, product of Invitrogen) to cause expression of the C2GnT-I, α4GnT, soluble CD43 and polyoma·virus large T antigen in the resulting CHO·Lec2 cells and contacting them with each other, whereby the soluble CD43 containing a terminal GlcNAcα residue can be expressed as the functional molecule.

In the third aspect of the production process, the first polynucleotide and, if needed, at least one of the second polynucleotide and the third polynucleotide are introduced into the embryo of a mammal other than humans.

The first polynucleotide is preferably introduced into an embryo in a way that it can mutually act with at least one of 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal. In such case, one or both of the second and third polynucleotides may be introduced into the embryo in a way that they can mutually act with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

No particular limitation is imposed on the gene relating to the mammary gland and it can be selected as needed depending on the using purpose. For example, mammary gland specific gene can be preferred.

No particular limitation is imposed on the 5' regulatory sequence and it can be selected as needed, depending on the using purpose. For example, 5' regulatory sequence having a promoter is preferred.

No particular limitation is imposed on the promoter and it can be selected as needed, depending on the using purpose. Preferred examples include whey acidic protein (WAP) promoter, α-casein promoter, β-casein promoter, γ-casein promoter, α-lactalbumin promoter and β-lactoglobulin promoter.

The term "it can mutually act on each other with" as used herein means "it is operatively linked with". Described specifically, two or more molecules work as one

unit and at the same time, form a mutual positional relationship permitting exhibition of effects by each molecule, all the molecules, or combination of them.

When the third polynucleotide encoding the polypeptide having at least one O-glycosylated region is introduced into a control element (for example, mammary gland specific promoter) in at least one of the 5' regulatory sequence and 3' regulatory sequence so that they are operatively linked, the control element controls the polynucleotide in a manner similar to that employed for another polynucleotide sequence related within the ordinary cells and the encoded polypeptide can be expressed tissue-specifically within mammary epithelial cells. It is also possible to introduce the first polynucleotide sequence in the second polynucleotide sequence so that they are operatively linked and to cause expression of two or more polypeptides from the polynucleotide thus introduced to be operatively linked. If necessary, a chimeric (combined) polypeptide can be expressed from the polynucleotide thus introduced to be operatively linked. The chimeric polypeptide may be a fused polypeptide. The fused polypeptide is a single polypeptide obtained by the translation of the above-described two or more encoded polypeptides, that is, a polypeptide obtained by covalent bonding of these polypeptides by a peptide bond.

The third polynucleotide is preferably introduced into an embryo to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing a polypeptide having at least one O-glycosylated region to be secreted in milk.

The milk may be obtained after causing the female offspring to produce it and the functional molecule may be isolated from the milk.

In the third aspect of the production process, the α4GnT expresses from the first polynucleotide in the body of the female offspring, and the endogenous or

exogenous polypeptide having at least one O-glycosylated region is glycosylated by at least either one of the C2GnT-I or C1-β3GnT, whereby the functional molecule can be produced. The functional molecule is contained in the milk of the female offspring so that it can be produced efficiently by milking.

In the above-described production process of the functional molecule according to the present invention, an isolation step may follow the production of the functional molecule.

The functional molecule of the present invention can be used in various fields. It can be suitably used for remedies for diseases caused by *Helicobacter pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, remedies for gastritis, or drugs for alleviating chronic gastritis), particularly for the composition, pharmaceutical and food or beverage of the present invention which will be described below.

(Composition, Pharmaceutical, and Food or Beverage) - The composition, pharmaceutical and food or beverage of the present invention each contains at least either one of the molecules and the functional molecule of the present invention and in addition, optionally contains another component selected as needed.

The molecule and functional molecule have already been described above.

No particular limitation is imposed on the content of the at least one of the molecules and functional molecule in the total amount of the composition, pharmaceutical, or food or drink of the present invention and it can be selected as needed, depending on the using purpose.

No particular limitation is imposed on the content of the molecule in the total amount of the composition of the present invention and it can be selected as needed,

depending on the using purpose. In general, the higher the content is, the higher the antibacterial effect becomes.

No particular limitation is imposed on the content of the functional molecule in the total amount of the composition of the present invention and it can be selected as needed, depending on the using purpose. In general, the higher the content is, the higher the antibacterial effect becomes.

No particular limitation is imposed on the content of the functional molecule in the total amount of the pharmaceutical of the present invention and it can be selected as needed, depending on the using purpose. In general, the higher the content is, the higher the antibacterial effect becomes.

No particular limitation is imposed on the content of the functional molecule in the total amount of the food or beverage of the present invention and it can be selected as needed, depending on the using purpose. In general, the higher the content is, the higher the antibacterial effect becomes.

(Other components) - No particular limitation is imposed on Other components and it can be selected as needed, depending on the using purpose. Examples include excipients, lubricants, binders, water soluble polymers, basic inorganic salts, solvents, solubilizing agents, suspending agents, isotonizing agents, buffering agents, soothing agents, antiseptics, antioxidants, coloring agents, sweeteners, acidulants, effervescents, and perfumes. For efficiently suppress or inhibit the synthesis of CGL, addition of a cholesterol degradative enzyme or glucose degradative enzyme is preferred.

Examples of the excipient include lactose, sucrose, D-mannitol, starch, corn starch, crystalline cellulose, light silicic anhydride and titanium oxide.

Examples of the lubricant include magnesium stearate, sucrose fatty acid ester, polyethylene glycol, talc, and stearic acid.

Examples of the binder include hydroxypropyl cellulose, hydroxypropyl methylcellulose, crystalline cellulose, starch, polyvinylpyrrolidone, gum arabic powder, gelatin, pullulan, and low-substituted hydroxypropyl cellulose.

Examples of the water soluble polymer include cellulose derivatives such as hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose and carboxymethylcellulose sodium, polyvinylpyrrolidone, sodium polyacrylate, polyvinyl alcohol, sodium alginate and guar gum.

Examples of the basic inorganic salt include basic inorganic salts with sodium, potassium, magnesium or calcium. Examples of the basic inorganic salt with sodium include sodium carbonate, sodium hydrogencarbonate and disodium hydrogenphosphate. Examples of the basic inorganic salt with potassium include potassium carbonate, and potassium hydrogencarbonate. Examples of the basic inorganic salts with magnesium include heavy magnesium carbonate, magnesium carbonate, magnesium oxide, magnesium hydroxide, magnesium aluminometasilicate, magnesium silicate, magnesium aluminate, synthetic hydrotalcite ($Mg_6Al_2(OH)_{16}\cdot CO_3\cdot 4H_2O$) and alumina oxide·magnesium. Examples of the basic inorganic salts with calcium include precipitated calcium carbonate and calcium hydroxide.

Examples of the solvent include distilled water for injection, alcohol, propylene glycol, macrogol, sesame oil, corn oil and olive oil.

Examples of the solubilizing agent include polyethylene glycol, propylene glycol, D-mannitol, benzyl benzoate, ethanol, tris-aminomethane, cholesterol, triethanolamine, sodium carbonate, and sodium citrate.

Examples of the suspending agent include surfactants such as stearyltriethanolamine, sodium lauryl sulfate, laurylaminopropionic acid, lecithin, benzalkonium chloride, benzethonium chloride and glycerin monostearate; and

hydrophilic polymers such as polyvinyl alcohol, polyvinylpyrrolidone, carboxymethylcellulose sodium, methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose and hydroxypropylcellulose.

Examples of the isotonizing agent include glucose, D-sorbitol, sodium chloride, glycerin and D-mannitol.

Examples of the buffering agent include phosphates, acetates, carbonates and citrates.

Examples of the soothing agent include benzyl alcohol.

Examples of the antiseptic include paraoxybenzoates, chlorobutanol, benzyl alcohol, phenethyl alcohol, dehydroacetic acid and sorbic acid.

Examples of the antioxidant include sulfites, ascorbic acid and α-tocopherol.

Examples of the coloring agent include food dyes such as Food Yellow No. 5, Food Red No. 2 and Food Blue No. 2, food lake dyes and red iron oxide.

Examples of the sweetener include saccharin sodium, dipotassium glycyrrhizinate, aspartame, stevia and thaumatin.

Examples of the acidulant include citric acid (citric anhydride), tartaric acid and malic acid.

Examples of the effervescent include sodium bicarbonate.

Examples of the perfume include extracts from lemon, lime, orange, menthol and strawberry.

No particular limitation is imposed on the using process for the composition or pharmaceutical of the present invention and it can be selected as needed, depending on the using purpose. For example, it may be orally administered. Alternatively, it may be directly sprayed or coated to the mucous layer of at least one of the human stomach or intestine.

The composition or pharmaceutical of the present invention may be used after impregnated in a film or sheet. The resulting film or sheet is preferably applied to at least either one of the stomach and intestine. Such administration is advantageous, because the composition or pharmaceutical sprayed or coated to the film or sheet can be maintained for a predetermined time without dropping therefrom over the surface of the mucous layer of the stomach or intestine, making it possible to administer the intended amount of the composition or pharmaceutical and have sufficient antibacterial effects. For the above-described using method, known medical instruments such as endoscope are preferably used.

No particular limitation is imposed on the using process for the composition or pharmaceutical and it can be selected as needed, depending on the using purpose. Examples of the using method include administration.

No particular limitation is imposed on the administration and it can be selected as needed, depending on the using purpose. For example, the composition or pharmaceutical may be orally administered. A liquid containing the functional molecule may be sprayed or coated to the mucous layer of the human stomach or intestine. Alternatively, either one of a sheet or film containing the functional molecule may be applied to the mucous layer of the stomach or intestine.

When the affected area is stomach, the film or sheet preferably contains chitin, sugar and a fat component. When the affected area is intestine, chitin is preferred. Incorporation of such a substance makes it possible to bring the functional molecule into contact with the affected area for long hours without causing decomposition of the molecule by the gastric or intestinal juice in the stomach or intestine.

The composition, pharmaceutical and food or beverage according to the present invention each has sufficient antibacterial effects. In order to improve the

effects further, at least one of known antibiotics and crude drugs which are remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, remedies for gastritis, or drugs for alleviating chronic gastritis may be used in combination.

Since the composition, pharmaceutical and food or beverage according to the present invention each contains the functional molecule (or the molecule) of the present invention, it is of great advantage with high safety and without side effects.

The composition of the present invention can be used in various fields. It can suitably be used for remedies for diseases caused by *Helicobacter pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, remedies for gastritis, and drugs for alleviating chronic gastritis), particularly for the pharmaceutical and food or beverage of the present invention.

The pharmaceutical of the present invention is especially suited for remedies for diseases caused by *Helicobacter pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*Helicobacter pylori* agents, and remedies for gastritis). Since it is free from side effects and has high safety, it is especially suited for the long-term use as a drug for alleviating chronic gastritis.

The food or beverage of the present invention can be used suitably for soft drinks, carbonated drinks, energy drinks, fruit juices, lactic acid beverages, dietary supplements, frozen deserts, noodles, confectionery, marine products, milk products, processed foods, seasonings, tablets and capsules.

(Transgenic mammals) - The transgenic mammal of the present invention is a transgenic mammal other than humans and capable of secreting milk, which has, as a genome, a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT), a second polynucleotide encoding at least either one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation

β1,3-N-acetylglucosaminyl transferase (C1-β3GnT) and a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

The first to third polypeptides, α4GnT, C2GnT-I, C1-β3GnT, and polypeptide having at least one O-glycosylated region have already been described.

The first to third peptides may each be exogenous or endogenous.

The first polynucleotide is preferably introduced into the genome so as to be operatively linked with at least either one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of mammals. In such case, one or both of the second and third polypeptides may be introduced into the genome so as to be operatively linked with at least either one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of mammals.

No particular limitation is imposed on the gene relating to the mammary gland and it can be selected as needed, depending on the using purpose. Preferred examples include a mammary gland specific gene.

The first to third polynucleotides may form one nucleic acid molecule and the nucleic acid molecule may be introduced into the genome so as to be operatively linked with at least either one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland.

No particular limitation is imposed on the 5' regulatory sequence and it can be selected as needed, depending on the using purpose. It preferably has a promoter.

No particular limitation is imposed on the promoter and it can be selected as needed, depending on the using purpose. Preferred examples include whey acidic protein (WAP) promoter, α-casein promoter, β-casein promoter, γ-casein promoter, α-lactalbumin promoter and β-lactoglobulin promoter.

The third polynucleotide is preferably introduced into a genome so as to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing secretion, in the milk, of a polypeptide having at least one O-glycosylated region.

No particular limitation is imposed on the kind of mammals and it can be selected as needed depending on the using purpose. Examples include mouse, rat, rabbit, horse, pig, sheep, goat and cow.

Whether one needs to introduce into the transgenic mammal the second exogenous polynucleotide or not is determined as follows. When cells producing the functional molecule of the present invention express the endogenous C2GnT-I under natural conditions, introduction of the second exogenous polynucleotide is not necessary. Whether one needs to introduce into the transgenic mammal the third exogenous polynucleotide or not is determined as follows. When cells producing the functional molecule of the present invention express the endogenous polypeptide having at least one O-glycosylated region under natural conditions, introduction of the third exogenous polynucleotide is not necessary. For example, when the cells are mammary epithelial cells, the mammary epithelial cells express the C2GnT-I and the polypeptide having at least one o-glycosylated region so that a transgenic mammal having the mammal epithelial cells do not necessarily need the second and third polynucleotides to be introduced therein.

In the transgenic mammals of the present invention, the polypeptide having at least one O-glycosylated region is glycosylated by the α4GnT and at least either one of the C2GnT-I and C1-β3Gn so that when they are females capable of secreting the milk, they can secret the functional molecule of the present invention in their milk.

The production process of a transgenic mammal which is other than humans and can secret a recombinant type polypeptide in its milk is known. The transgenic mammal can be produced by such a known method (for example, USP 6,344,596, 6,548,735, 6,222,094, 5,962,648, 5,891,698, 5,850,000, etc.)

(Methods of suppressing growth of bacteria, treating or preventing gastric ulcer, and treating gastric cancer) - The process for suppressing growth of bacteria according to the present invention comprises bringing bacteria requiring cholesteryl-α-D-glucopyranoside (CGL) into contact with a functional molecule having at least one α1,4-N-acetylglucosamine residue to suppress or inhibit at least either one of growth of the bacteria or formation of cell walls of the bacteria.

The process for treating gastric ulcer according to the present invention comprises administering a functional molecule having an α1,4-N-acetylglucosamine residue to alleviate signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* bacteria.

The process for preventing gastric ulcer according to the present invention comprises administering a functional molecule having an α1,4-N-acetylglucosamine residue to prevent signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* bacteria.

The process for treating gastric cancer according to the present invention comprises administering a functional molecule having an α1,4-N-acetylglucosamine residue to alleviate signs or symptoms of gastric cancer induced by the infection of a subject with *Helicobacter* bacteria.

No particular limitation is imposed on the functional molecule and it can be selected as needed, depending on the using purpose. For example, gland mucous cell-type mucin is preferred, with the functional molecule of the present invention being

especially preferred. The functional molecule capable of suppressing or inhibiting enzymatic activity of UDP-Glc:sterol glycosyltransferase is preferred. Such a molecule can suppress or inhibit the synthesis of the CGL from cholesterol by the aid of the UDP-Glc:sterol glycosyltransferase. This results in efficient suppression or inhibition of at least either one of the growth of the bacteria and formation of cell walls of the bacteria.

No particular limitation is imposed on the subject and it can be selected as needed, depending on the using purpose. For example, mammals are preferred, with human beings being more preferred.

Examples of the mammals include mouse, rat, rabbit, horse, pig, sheep and cow.

No particular limitation is imposed on the *Helicobacter* bacteria and they can be selected as needed, depending on the using purpose. For example, *Helicobacter pylori* are preferred.

No particular limitation is imposed on the administration route and it can be selected as needed, depending on its purpose. For example, the functional molecule may be orally administered. A liquid containing the functional molecule may be sprayed or coated to the mucous layer of the stomach. Alternatively, either a film or sheet containing the functional molecule may be applied to the mucous layer of the stomach.

The film or sheet preferably contains chitin, sugar and fat component. Incorporation of such a substance makes it possible to bring the functional molecule into contact with an affected area for long hours without being degraded by the gastric juice in the stomach.

As the functional molecule to be used for administration, the composition, pharmaceutical or food or beverage of the present invention is preferably used. Milk produced by the production process of the functional molecule of the present invention is also preferably employed. The milk can be used as milk products (for example, cheese, butter and yogurt) by further processing.

Examples of the present invention will be described below. It should however be borne in mind that the present invention is not limited to or by them.

Example 1

Production of CD43 containing, at the terminal thereof, an α type N-acetylglucosamine residue -

In an α-MEM medium containing 10% fetal calf serum (FCS), Chinese hamster ovary cell mutant (CHO·Lec2 cells) deficient in a CMP-sialic acid transporter was cultured.

By amplifying a DNA fragment (a portion corresponding to the 20th to 254th amino acids of the amino acid sequence of SEQ. ID. No. 1 (Minoru Fukuda, "Leukosialin, a major sialoglycoprotein defining leukocyte differentiation" 1989 Carbohydrate recognition in cellular function. Wiley, Chichester (Ciba Foundation Symposium 145) 257-276)) including the whole extracellular domain of the CD43 by the PCR method and subcloning the amplified DNA fragment into pSecTag2 (product of Invitrogen), Igκ leader peptide, myc epitope following it and a vector (pSecTag2-sCD43) encoding $(His)_6$ were produced.

Then, four vectors having, incorporated in the pSecTag2-sCD43,(1) cDNA encoding core 2β1,6-N-aceteylglucosaminyl transferase-I (C2GnT-I), (2) cDNA encoding α1,4-N-acetylglucosaminyl transferase (α4GnT), and (3) cDNA encoding a polyoma virus large T antigen, respectively are transfected into the cultured CHO·Lec2

cells using LipofectAmine (trade mark, product of Invitrogen) to cause expression of soluble CD43 containing a terminal GlcNAcα residue in the transfected CHO·Lec2 cells, whereby the GlcNAcα-CD43 was produced.

The GlcNAcα-CD43 thus produced were subjected to measurement of GlcNAcα-CD43 activity with a commercially available ELISA kit (ELISA kit for gastric gland mucous cell-type mucin measurement, available from Kanto Kagaku) using an HIK1083 antibody (HIK1083 latex for gastric mucin detection, available from Kanto Kagaku) specific to the GlcNAcα residue (See, for example, A new diagnostic method for adenoma malignum and related lesions: latex agglutination test with a new monoclonal antibody, HIK1083, Clinica Chimica Acta 312 (2001) 231-233). For coloring reaction, ELISA ELAST amplification system (Perkin Elmer) was used. Coloring was observed, and the expression of a terminal GlcNAcα residue was confirmed. Further, quantification of protein was performed using a commercially available quantification system (BCA Protein Assay Kit, Pierce Biotechnology, Inc., Cat No. 23225, 23227). As a result, it was revealed that the number of the side chains (sugar chains) of the GlcNAcα-CD43 relative to each main chain (CD43) was 80 and that the sugar chains exist in the cluster form relative to the main chain. Additional analysis of the sugar chain using another commercially available quantification kit (Glycoprotein Carbohydrate Estimation Kit, Pierce Biotechnology, Inc., Cat No. 23260) revealed that the sugar chain is formed of GlcNAcα1 → 4Gal1β1 → 4GlcNAcβ1 →6(GlcNAcα1 → 4Galβ1 →3)GalNAcα → Ser/Thr; its branch number of the sugar chain is 1; and the number of monomer units is 6. The term "Ser/Thr" means bonding to either one of serine (Ser) or threonine (Thr) in CD43 serving as the main chain.

The transfected CHO·Lec2 cells succeeded in efficient synthesis of the CD43 by the polyoma·virus large T-antigen. The cDNA encoding the α4GnT was produced in accordance with the method as described in JP-A No. 2001-46077.

- Production of CD43 free of an α type N-acetylglucosamine residue -

For the measurement of control, soluble CD43 having no GlcNAcα residue in a core 2 branched O-glycan was produced in a similar manner to that employed for the production of the GlcNAcα-CD43 except for the use of a pcDNAI vector (product of Invitrogen) not having cDNA of the α4GnT incorporated therein.

The GlcNAcα-free CD43 thus produced were subjected to condensation reaction using a latex particle antibody specific to the GlcNAcα residue. No condensation was observed. As a result, it was revealed that the GlcNAcα-free CD43 did not contain a GlcNAcα residue. A further analysis of sugar chains revealed that the side chain (sugar chain) of CD43 not containing the GlcNAcα is formed of Galβ1 → 4GlcNAcβ1 →6(Galβ1 →3)GalNAcα → Ser/Thr. The "Ser/Thr" means bonding to either one of serine (Ser) or threonine (Thr) in CD43 serving as the main chain.

The growth, motility and abnormal morphologies of bacteria, and suppression or inhibition of CGL biosynthesis by a GlcNAcα residue were evaluated in the below-described manners by using the GlcNAcα-residue-containing soluble CD43, and GlcNAcα-residue-free CD43.

<Growth of bacteria>

By the microbroth dilution method, *Helicobacter pylori* (ATCC43504) was pre-cultured on a Brucella medium (Becton Dickinson Microbiology Systems) containing 10% horse serum. The *Helicobacter pylori* diluted to 1×10^7 cells/ml and GlcNAcα-CD43 having the concentration as shown in FIG.2A was charged in a 96-well plate, followed by culturing for 4 days under conditions of 35°C and 15% CO_2. In FIG.

2A, "αGlcNAc (+)" means that the GlcNAcα-CD43 is contained in the medium, while "αGlcNAc (-)" means that the soluble CD free of a GlcNAcα residue is contained in the medium. The concentration of the soluble CD free of a GlcNAcα residue in the medium is 125.0 mU/ml.

Growth of the *H. pylori* thus cultured was measured under the condition of OD600 nm by using a microplate spectrophotometer ("SPECTRAmax PLUS 384", product of Molecular Device). The results are shown in FIG. 2A. The minimum inhibitory concentration was measured in a similar manner to that employed above except for the use of Muller Hinton medium (product of Eiken Chemical) instead of the Brucella medium, whereby similar results were produced.

As a result, as illustrated in FIG. 2A, growth for the first 2.5 days was slight irrespective of the presence or absence of the GlcNacα residue, which is a characteristic of the growth induction period of *H. pylori*. On Day 3 after incubation, the growth period started and drastic growth of *H. pylori* was observed on the medium containing the soluble CD43 free of the GlcNacα residue. It has been proved that growth of *H. pylori* was suppressed or inhibited by the incubation with the GlcNacα-CD43. The unit "1 mU" is equivalent to 1 μg of p-nitrophenyl-N-acetylglucosamine (GlcNacα-PNP).

<Motility of Bacteria>

On a Brucella medium containing 31.2 mU/ml of GlcNAcα-CD43. *H. pylori* was cultured for 3 days. In order to study the motility of the *H. pylori* thus cultured, a time-lapse photograph of it was taken at an interval of 1 second through a confocal laser scanning microscope ("LSM510 META", product of Carl Zeiss) and the typical *H. pylori* was indicated by an arrow. The result is shown in Table 1B. A photograph

was taken in a similar manner except for the use of a Brucella medium containing the soluble CD43 free of a GlcNAcα residue and the result is shown in Table 1A.

In FIG. 2B, "αGlcNAcα (+)" means that the GlcNAcα-CD43 is contained in the medium, while "αGlcNAcα (-)" means that the soluble CD43 free of a GlcNAcα residue is contained in the medium. In each case, its concentration is 31.2 mU/ml. The underline on the right bottom of FIG. 2B represents 50 μm and all the pictures are time-lapse photographs taken at equal magnifications.

As a result, an average velocity of seven *H. pylori* cultured on the GlcNAcα-CD43-containing medium (αGlcNAcα (+)) was 3.1 ± 3.5 μm/sec, while that of seven *H. pylori* cultured on the medium (αGlcNAcα (-)) containing the CD43 free of a GlcNAcα residue was 21.1 ± 2.6 μm/sec. The significance by a t test was $P < 0.001$. Accordingly, it has been found that the motility of *H. pylori* decreases drastically on the GlcNAcα-CD43-containing medium.

<Appearance of Abnormal morphologies of Bacteria>

On a Brucella medium containing the GlcNAcα-CD43 or the soluble CD43 free of a GlcNAcα residue at a concentration of 31.2 mU/ml, *H. pylori* was cultured for 3 days. The SEM photograph of the *H. pylori* thus cultured was taken under the condition of accelerating voltage of 15 kV by using a scanning electron microscope ("JSM-6360LV", product of JEOL). The results are shown in Table 1C.

In Table 1C, "αGlcNAc (+)" means that the GlcNAcα-CD43 is contained in the medium, while "αGlcNAc (-)" means that the soluble CD43 free of a GlcNAcα residue is contained in the medium. In each case, its concentration is 31.2 mU/ml. The underline on the right bottom of FIG. 2C represents 1 μm and all the pictures are SEM photographs taken at equal magnifications.

As a result, abnormal morphologies such as elongation, narrowing and bending were observed in *H. pylori* cultured on the GlcNAcα-CD43-containing medium (αGlcNAcα (+)), while no abnormal morphologies were observed from the *H. pylori* cultured on the medium containing CD43 free of a GlcNAcα residue (αGlcNAcα (-)).

<Inhibition of CGL biosynthesis>

The inhibition of CGL biosynthesis by the GlcNAcα residue was analyzed in the below-described manners in two cases, that is, (1) CGL biosynthesis of *H. pylori* in vivo and (2) CGL biosynthesis in vitro.

<Inhibition of CGL biosynthesis of *H. pylori* in vivo>

- Synthesis of CGL by *H. pylori* in the presence of GlcNAcα-CD43 -

By using cholesterol and UDP-glucose, CGL was synthesized by *H. pylori* in the presence of GlcNAcα-CD43. The CGL thus biosynthesized in *H. pylori* in vivo was subjected to MALDI-TOF mass analysis.

After pre-culturing of *H. pylori* (ATCC43504) on a Brucella medium (Becton Dickinson Microbiology Systems) containing 10% horse serum, the *H. pylori* diluted to 1×10^7 cells/ml and GlcNAcα-CD43 adjusted to have a concentration of 4.0 mU/ml were charged in a 96-well plate, followed by culturing for 2 days at 35°C. The *H. pylori* thus cultured were collected, washed three times with PBS (free of Ca^{2+} and Mg^{2+}), and suspended in 1 ml of distilled water. The resulting suspension was centrifuged for 10 minutes at 6000 rpm, whereby cells were obtained.

The resulting cells were extracted overnight at 4°C in 2 ml of a chloroform·methanol mixture (2:1, by mass) mixture. The extract was filtered, followed by drying in a nitrogen gas stream. The dried sample thus obtained was dissolved in 4 ml of a chloroform·methanol mixture (2:1, by mass). In accordance with the process for Folch et al., 1 ml of water was added to the solution. The lower

phase of the resulting mixture was dried in a nitrogen gas stream and then, treated with 1 ml of a 0.5N sodium hydroxide·methanol solution for 1 hour at 50°C. After neutralization with a 6N aqueous solution of hydrochloric acid, 1 ml of petroleum ether was added to a reaction tube. After removal of the upper phase, 2 ml of petroleum ether was added to the lower phase. The lower phase was dried and then dissolved in 1 ml of a chloroform·methanol·water mixture (86:14:1, by mass) (TLP). To the same reaction tube, 0.5 ml of another chloroform·methanol·water mixture (3:48:47, by mass) (TUP) was added. From the resulting mixture, the lower phase was collected, dried in a nitrogen gas stream and then dissolved in 50 μl of chloroform.

In the next place, 1 μl of the sample was weighed, followed by the addition of 1 μl of 2,5-dihydroxybenzoic acid or 1 μl of trans-3-indoleacrylic acid. The resulting mixture was employed as a matrix. The mass spectrum of the sample was measured using Voyager-DE STR Biospectrometry Workstation DE MALDI-TOF MS (product of PE Applied Biosystems) in a positive ion or negative ion reflector mode at laser intensity of 2300. External calibration with 2 points was conducted with phosphatidic acid internally appearing in *H. pylori* as an internal standard. The results are shown in FIG. 2B.

As a control, the mass spectrum of CGL was measured in a similar manner except for the use of the CD43 free of a GlcNAcα residue instead of the GlcNAcα-CD43. The results are shown in FIG. 3A.

As shown in FIGS. 3A and 3B, a peak of CGL was detected at m/z of 571.6 both in the presence of the GlcNAcα-CD43 and in the presence of the CD43 free of a GlcNAcα residue. The peak of CGL in the presence of the GlcNAcα-CD43 however showed a drastic decrease to 29.5% compared with the peak of CGL measured in the control.

The results have revealed that the GlcNAcα-CD43 inhibited biosynthesis of CGL in *H. pylori* in vivo.

<<Inhibition of Biosynthesis of CGL in vitro>>

- Synthesis of CGL by *H. pylori* in the presence of GlcNAcα-CD43 -

By using cholesterol and UDP-glucose, CGL was synthesized by sonicated *H. pylori* and MALDI-TOF mass spectrometry of the CGL synthesized in vitro was performed in the below-described manner.

After pre-culturing of *H. pylori* (ATCC43504) on a Brucella medium (Becton Dickinson Microbiology Systems) containing 10% horse serum, the *H. pylori* diluted to 5×10^7 cells/ml was cultured on a Brucella medium added with 5% horse serum at 35°C for 2 days. A 2 ml portion of the *H. pylori* (5×10^7 cells/ml) thus cultured was collected, washed three times with PBS (free of Ca^{2+} and Mg^{2+}), and suspended in 1 ml of distilled water. The resulting suspension was centrifuged for 10 minutes at 6000 rpm, whereby a lipid component was obtained.

In 1 ml of a reaction buffer containing 100 mM Tris buffer (pH 7.5), 15 mass% of glycerol, 5 mM DTT, 200 μM Pefabloc (product of Merck) and 0.5 mg/ml of lysozyme, *H. pylori* was suspended, followed by culturing at 20°C for 5 minutes. On an ice bath, the sample was sonicated 10 times in an ultrasonic water bath at intervals of 30 seconds. Then, 100 μl of a reaction mixture containing 80 μl of the sonicated *H. pylori*, 5 μl of a 8 mM cholesterol ethanol solution, 5 μl of 7.2 μM UDP-Glc (UDP-glucose), 1 μl of Triton CF-54 (Sigma Chemical Co., St. Louis, MO, USA) and 9 μl of the reaction buffer was allowed to stand (incubated) at a fixed temperature of 30°C for 3 hours. The reaction was then terminated by the addition of 900 μl of a 0.45% NaCl solution and 4 ml of a 2:1 chloroform:methanol mixture.

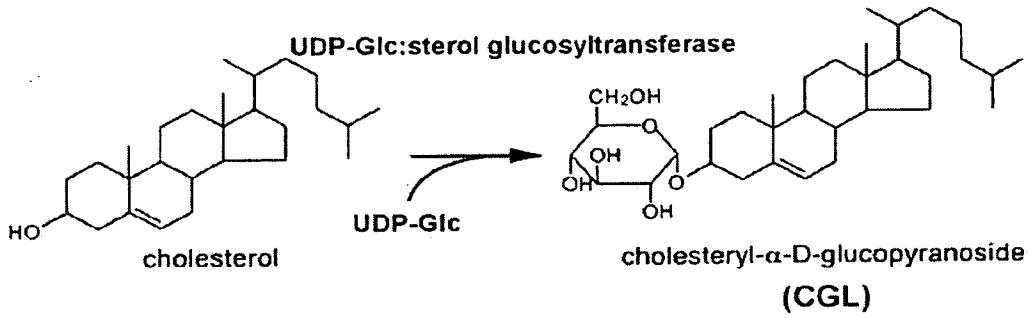
From the resulting mixture, the lower phase was filtered, followed by drying in a nitrogen gas stream. The lipid sample thus obtained by drying was dissolved in 4 ml of a chloroform·methanol mixture (2:1, by mass). In accordance with the process for Folch et al., 1 ml of water was added to the solution. The lower phase of the resulting mixture was dried in a nitrogen gas stream and then, treated with 1 ml of a 0.5N sodium hydroxide·methanol solution for 1 hour at 50°C. After neutralization with a 6N aqueous solution of hydrochloric acid, 1 ml of petroleum ether was added to a reaction tube. The upper phase was removed and then, 2 ml of petroleum ether was added to the lower phase. The lower phase was dried and then dissolved in 1 ml of a chloroform·methanol·water mixture (TLP) (86:14:1, by mass). To the same reaction tube, 0.5 ml of another chloroform·methanol·water mixture (TUP) (3:48:47, by mass) was added. From the resulting mixture, the lower phase was collected, dried in a nitrogen gas stream and then dissolved in 50 μl of chloroform.

In the next place, 1 μl of the sample was weighed, followed by the addition of 1 μl of 2,5-dihydroxybenzoic acid or 1 μl of trans-3-indoleacrylic acid. The resulting mixture was employed as a matrix. The mass spectrum of CGL was measured using Voyager-DE STR Biospectrometry Workstation DE MALDI-TOF MS (product of PE Applied Biosystems) in a positive ion reflector mode at laser intensity of 2500. External calibration with 2 points was conducted with phosphatidic acid internally appearing in *H. pylori* as an internal standard. The results are shown in FIG. 3C.

In a similar manner to that employed above except that 5.0 mU of GlcNAcα-CD43 was added to the reaction buffer, the mass spectrum of CGL was measured. The results are shown in FIG. 3D. Further, in a similar manner to that employed above except that 5.0 mU of CD43 free of a GlcNAcα residue was added to

the reaction buffer, the mass spectrum of CGL was measured. The results are shown in FIG. 3E.

The sample synthesized by the sonicated H. pyroli by using UDP-Glc and cholesterol was subjected to MALDI-TOF mass spectrometry, resulting in the detection of a peak of CGL at m/z of 571.6 as is apparent from FIG. 3C. This is presumed to occur because *H. pylori* has an activity of UDP-Glc:sterol glucosyltransferase for transferring UDP-Glc to the C3 position of cholesterol as illustrated in the below-described scheme.



No peak of CGL was however detected at m/z of 571.6 as illustrated in FIG. 3D when incubation was conducted similarly in the presence of the GlcNAcα-CD43. When incubation was conducted in a similar manner in the presence of the CD43 free of a GlcNAcα residue instead of the GlcNAcα-CD43, a peak of CGL was detected at m/z of 571.6, and not difference was found from the peak of CGL when neither the GlcNAcα-CD43 nor the CD43 free of a GlcNAcα residue was added. These results have revealed that the GlcNAcα residue inhibited biosynthesis of CGL.

The formation mechanism of the cell walls of *H. pylori* including identification of glycosyltransferase relating to the biosynthesis of α-CGS has not yet been elucidated. In consideration of the similarity in structure of the GlcNAcα residue and α-binding type Glc contained in CGL, however, the above-described analysis results suggest that

biosynthesis of CGL may be inhibited by the competition between the GlcNAcα residue and UDP-Glc for a donor substrate of UDP-Glc:sterol glycosyltransferase or by the direct inhibition against UDP-Glc:sterol glycosyltransferase by the final product inhibiting mechanism of the GlcNAcα residue.

Based on the evaluation results of growth, motility, appearance of abnormal morphologies of bacteria and suppression or inhibition of CGL biosynthesis by the GlcNAcα residue, it has been understood that administration of a functional molecule having an α1,4-acetylglucosamine residue alleviates or prevents the signs or symptoms of gastric ulcer or gastric cancer induced by the infection of subjects with *Helicobacter* bacteria.

(Experimental example 1)

Tests were performed to examine the survival of *H. pylori* in the presence or absence of cholesterol and synthesis of CGL by *H. pylori*.

<Surviving condition of *H. pylori* in the presence or absence of cholesterol>

Genes relating to the biosynthesis of cholesterol have not yet been discovered from the genomic data of *H. pylori*. Considering the possibility that *H. pylori* cannot synthesize CGL without exogenous cholesterol, the following test was conducted. Described specifically, when *H. pylori* (ATCC43504) was cultured on an Ham's F-12 medium free of cholesterol for 5 days under the standard anaerobic conditions at 35°C, growth of *H. pylori* was suppressed to the level of 50% of that cultured on an Ham's F-12 medium containing cholesterol under similar conditions. The results are shown in Table 1.

H. pylori did not show motility on the cholesterol-free medium but abnormal extension (abnormal morphology) was observed as is apparent from the left side of

FIG. 2C. The *H. pylori* died out completely when cultured for further 21 days in the absence of cholesterol.

When cultured on a cholesterol-added medium, on the other hand, *H. pylori* growth was smooth and no abnormal morphology was discovered (Table 1). It has been understood from these results that synthesis of CGL using cholesterol is necessary for the survival of *H. pylori*.

Table 1

	In the presence of cholesterol	**In the absence of cholesterol**	
	5 Days	**5 Days**	**21 Days**
Colony formation (CFU/ml)	**1×10^8**	**5×10^7**	**No growth**
Motility	**Good**	**None**	-
Morphology	**Normal**	**Abnormal**	-

<Synthesis of CGL by *H. pylori*>

The expression level of CGL in *H. pylori* in the presence or absence of cholesterol was studied by analyzing, as described below, variations in the expression level of αCGs containing CGL at the glycolipid portion of *H. pylori* through thin-film chromatography (TLC).

From a Brucella medium containing cholesterol and a cholesterol-free medium on each of which *H. pylori* had been cultured, 1×10^8 cells/ml of *H. pylori* were collected and the glycolipid portion thereof was extracted over 1 hour at room temperature by using a 2:1 (mass ratio) mixture of chloroform and methanol. The extract was dried under a nitrogen gas stream, followed by thin-film chromatography (TLC) with a 16:6:1 (mass ratio) mixture of chloroform, methanol and water. The glycolipid portion thus separated was visualized by staining with an orcinol sulfate buffer at 110°C. The results are shown in FIG. 4. In FIG. 4, Lane 1 shows the

analysis results of the glycolipid portion extracted from *H. pylori* cultured on a cholesterol-free Brucella medium, while Lane 2 shows the analysis results of the glycolipid portion extracted from *H. pylori* cultured on a cholesterol-containing Brucella medium.

As a result, three adjacent lines typical of CGL-containing α-CGs, which lines are characteristic of *H. pylori*, were detected when *H. pylori* was cultured on a cholesterol-containing medium (Lane 2). On the other hand, no α-CGs (CGL) was detected when *H. pylori* was cultured on a cholesterol-free medium (Lane 1).

Example 2

Production of CD34 containing an α type N-acetylglucosamine residue -

In a similar manner to Example 1 except that pcDNA3 (product of Invitrogen) was used instead of pSecTag2, and pcDNA3-CD34-IgG encoding soluble CD34-IgG chimera was used instead of cDNA encoding soluble CD43, soluble CD34 containing a GlcNAcα residue was produced. The growth, motility and appearance of abnormal morphologies of bacteria were analyzed and inhibition of CGL biosynthesis by the GlcNAcα residue was evaluated, each in a similar manner to Example 1, whereby similar results to those of Example 1 were obtained.

Example 3

Production of AGS cells expressing CD43 containing an α type N-acetylglucosamine residue

In a similar manner to Example 1 except for the use of gastric adenocarcinoma cells (AGS cells) instead of CHO·Lec2 cells, AGS-α4GnT cells stably expressing GlcNAcα-CD43 were produced.

Production of AGS cells expressing CD43 not containing an α type N-acetylglucosamine residue -

In a similar manner to that employed for the production of AGS-α4GnT cells except that a pcDNAI vector (product of Invitrogen) having the α4GnT-enconding cDNA not incorporated therein was used, Mock-transfected AGS cells stably expressing CD43 not containing a GlcNAcα residue was produced for the measurement of control.

The AGS-α4GnT cells or Mock-transfected AGS cells thus produced were co-cultured with 1×10^7 cells/ml of *H. pylori* ( ) for 24 hours. The cells thus cultured were photographed by a Nomarski microscope. The results are shown in the lower part of FIG. 5.

After immobilization with 20% buffer formalin, the AGS-α4GnT cells or Mock-transfected AGS cells were incubated together with a mixture of a rabbit polyclonal antiserum (DAKO) against *H. pylori* and mouse monoclonal HIK1083 antibody (product of Kanto Chemical), followed by fluorescent staining with the mouse monoclonal HIK1083 antibody. As the secondary antibody, rhodamine-labeled anti-rabbit immunoglobulin (for anti-*H. pylori* antibody) and fluorescein isothiocyanate-labeled antimouse IgM (for HIK1083 antibody) were added and a slide was made. The slide was sealed with Vectashield (product of Vector Laboratories) and photographed by a confocal laser scanning microscope ("LSM510 META", product of Carl Zeiss). The results are shown in the upper part of FIG. 5.

On the upper right of FIG. 5, shown is a photograph of the fluorescent-stained AGS-α4GnT cells. A portion in white represents the fluorescent-stained HIK1083 antibody and it has been confirmed that the HIK1083 antibody surrounds the AGS-α4GnT cells. The HIK1083 antibody is specific to the GlcNAcα residue, suggesting the expression of the GlcNAcα residue by the AGS-α4GnT cells. As

illustrated in the lower right of FIG. 5, no cellular damage was observed in the AGS-α4GnT cells in which the GlcNAcα residue has been expressed.

In the upper left of FIG. 5, shown is a photograph of the Mock-transfected AGS cells which were fluorescent- stained in a similar manner to that employed for the AGS-α4GnT cells. A portion in white represents *H. pylori* and it has been confirmed that *H. pylori* exists to surround the Mock-transfected AGS cells and that the GlcNAcα residue has not been expressed because of the absence of the fluorescent-stained HIK1083 antibody. As illustrated in the lower left of FIG. 5, a remarkable cellular damage was observed in the AGS-α4GnT cells in which no GlcNAcα residue has been expressed.

Example 4

According to a known process of enzyme synthesis (see, for example, Murata, T. & Usui, T. Trends Glycosci. Glycotech., 12, 161-174 (2000), a sugar chain consisting of 6 residues, GlcNAcα1 → 4Ga1β1 → 4GlcNAcβ1 →6(GlcNAcα1 → 4Galβ1 →3)GalNAcα, was produced. In a similar manner to Example 1, growth, motility and appearance of abnormal morphologies of bacteria were analyzed and inhibition of CGL biosynthesis by a GlcNAcα residue were evaluated, whereby similar results to those of Example 1 were obtained.

Considering all the above-described results of Examples 1 to 4 and Test 1 together, CGL is indispensable for the growth of *H. pylori* and the GlcNAcα residue exhibits an antibacterial property against *H. pylori* by inhibiting biosynthesis of CGL. It is presumed that the antibacterial property of a sugar chain containing the GlcNAcα residue or a functional molecule containing this sugar chain is limited only to bacteria species expressing CGL.

The molecule of the present invention contains a molecule of mucin existing in the human gastric mucosa and the functional molecule of the present invention contains the mucin so that they have high safety without side effects. The molecule, functional molecule or composition containing it according to the present invention can be used suitably as a pharmaceutical, or food or beverage.

The conventional problems can be overcome by the present invention and it is possible to provide a molecule, functional molecule, composition, pharmaceutical, food or beverage, milk having an antibacterial effects (for example, inhibiting or disturbing growth and motility of bacteria requiring CGL and causing abnormal morphologies of the bacteria), having no side effects and being excellent in safety; and transgenic mammals capable of producing the functional molecule. The present invention can also provide an efficient production process of the functional molecule, and a treating process for gastric cancer, treating process for gastric ulcer and preventing process for gastric ulcer each having sufficient effects to kill bacteria, having no side effects and being excellent in safety.

The molecule, functional molecule, composition and pharmaceutical according to the present invention are preferably employed for remedies for diseases caused by *H. pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*H. pylori* agents, remedies for gastritis and drugs for alleviating chronic gastritis). The pharmaceutical according to the present invention has no side effects and high safety so that it can be suited as remedies for diseases caused by *H. pylori* (for example, remedies for gastric ulcer, remedies for duodenal ulcer, anti-*H. pylori* agents, and remedies for gastritis). Owing to high safety without side effects, it is suited for long-term use as a drug for alleviating chronic gastritis. The food or beverage, and milk according to the present invention can be suited for use as soft drinks, carbonated

drinks, energy drinks, fruit juices, lactic acid beverages, dietary supplements, frozen deserts, noodles, confectionery, marine products, milk products, processed foods, seasonings, tablets and capsules. The transgenic mammals of the present invention can be suited for use in the production of the functional molecule and milk of the present invention, because they can efficiently produce the functional molecule and milk of the present invention. The production process of the functional molecule according to the present invention permits efficient production of it, so that the process can be used preferably for the production of the functional molecule of the present invention.

What is claimed is:

1. A molecule, comprising a plurality of monomer units, wherein at least one of the monomer units is an N-acetylglucosamine residue.

2. A molecule according to Claim 1, wherein the molecule is a sugar chain.

3. A molecule according to Claim 1, wherein the N-acetylglucosamine residue exists at a terminal of the molecule.

4. A molecule according to Claim 1, wherein the N-acetylglucosamine residue is an α1,4-N-acetylglucosamine residue.

5. A molecule according to Claim 1, further comprising a galactose residue, wherein the galactose residue exists adjacent to the N-acetylglucosamine residue.

6. A molecule according to Claim 1, which is at least one of linear and branched.

7. A composition, comprising a molecule according to Claim 1.

8. A composition according to Claim 7, to be used for one of a pharmaceutical and edible composition.

9. A functional molecule, comprising a molecule according to Claim 1.

10. A functional molecule according to Claim 9, comprising a main chain and a side chain, wherein the side chain is the molecule according to Claim 1.

11. A functional molecule according to Claim 10, wherein the main chain is a polypeptide.

12. A functional molecule according to Claim 9, wherein the molecule according to Claim 1 exists in the cluster form relative to the main chain.

13. A functional molecule according to Claim 9 capable of suppressing or inhibiting the synthesis of cholesteryl-α-D-glucopyranoside (CGL).

14. A functional molecule according to Claim 11, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

15. A functional molecule according to Claim 10, wherein a ratio of the number of the side chain to the main chain is 10 or more.

16. A functional molecule according to Claim 9 to be used for at least one of a remedy for gastric ulcer, a remedy for duodenal ulcer, an anti-*H. pylori* agent, a remedy for gastritis, and a drug for alleviating chronic gastritis.

17. A functional molecule according to Claim 9 to be used for an edible composition.

18. A composition, comprising a functional molecule according to Claim 9.

19. A pharmaceutical, comprising a functional molecule according to Claim 9.

20. A pharmaceutical according to Claim 19, which is sprayed or coated to the mucous layer of at least one of the stomach and intestine.

21. A pharmaceutical according to Claim 19 to be used after impregnated or incorporated in at least one of a film and a sheet.

22. A pharmaceutical according to Claim 21, wherein the at least one of a film and sheet is applied to the mucous layer of at least one of the stomach and intestine.

23. A pharmaceutical according to Claim 19, comprising at least one of a cholesterol degradative enzyme and a glucose degradative enzyme.

24. An edible composition, which comprises a functional molecule according to Claim 9.

25. A process for producing a functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising the step of:

contacting

α1,4-N-acetylglucosaminyl transferase (α4GnT),

at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a polypeptide having at least one O-glycosylated region, thereby producing a functional molecule having at least one α1,4-N-acetylglucosamine residue.

26. A process for producing a functional molecule according to Claim 25, wherein the polypeptide is a soluble polypeptide.

27. A process for producing a functional molecule according to Claim 25, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

28. A process for producing a functional molecule according to Claim 25, wherein the polypeptide is mucin secreted into milk of mammals.

29. A process for producing a functional molecule according to Claim 25, further comprising isolating the functional molecule having at least one α1,4-N-acetylglucosamine residue after production thereof.

30. A functional molecule obtained by a process for producing a functional molecule according to Claim 25.

31. A process for producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising:

expressing, in a eukaryotic cell,

a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT),

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

32. A process for producing a functional molecule according to Claim 31, wherein at least one of the first, second and third polynucleotides is an exogenous one introduced into the eukaryotic cell.

33. A process for producing a functional molecule according to Claim 31, wherein the polypeptide is a soluble polypeptide.

34. A process for producing a functional molecule according to Claim 31, wherein the polypeptide is at least one of CD43, CD34 and Muc-6.

35. A process for producing a functional molecule according to Claim 31, wherein the eukaryotic cell is a cell of a mammal.

36. A process for producing a functional molecule according to Claim 31, further comprising:

contacting

the α4GnT-I,

at least one of the C2GnT-I and the C1-β3GnT, and

the polypeptide having at least one O-glycosylated region, after expressing,

thereby producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue.

37. A process for producing a functional molecule according to Claim 36, further comprising isolating the recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue after production thereof.

38. A functional molecule obtained by a process for producing a functional molecule according to Claim 31.

39. A transgenic mammal other than humans and capable of secreting milk, wherein its genome comprises:

a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT);

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT); and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

40. A transgenic mammal according to Claim 39, wherein at least one of the first polynucleotide, second polynucleotide and third polynucleotide is an exogenous polynucleotide.

41. A transgenic mammal according to Claim 39, wherein at least one of the first polynucleotide, second polynucleotide and third polynucleotide is introduced into the genome so as to be linked operatively with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

42. A transgenic mammal according to Claim 39, wherein the third polynucleotide is introduced into the genome so as to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing the polypeptide having at least one O-glycosylated region to be secreted in the milk.

43. A transgenic mammal according to Claim 41, wherein the 5' regulatory sequence has a promoter.

44. A transgenic mammal according to Claim 43, wherein the promoter is at least one promoter selected from whey acidic protein (WAP) promoter, α-casein promoter, β-casein promoter, γ-casein promoter, α-lactalbumin promoter and β-lactoglobulin promoter.

45. A transgenic mammal according to Claim 39, wherein the first, second and third polynucleotides form one nucleic acid molecule and the nucleic acid molecule is introduced into the genome so as to be operatively linked with either one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating the mammary gland.

46. A transgenic mammal according to Claim 39, wherein the mammal is one of mouse, rat, rabbit, horse, pig, sheep, goat and cow.

47. A process for producing a recombinant functional molecule having at least one α1,4-N-acetylglucosamine residue, comprising:

introducing a first polynucleotide encoding α1,4-N-acetylglucosaminyl transferase (α4GnT) into an embryo of a mammal other than humans;

transplanting the embryo to a recipient female mammal;

causing the recipient female mammal to produce offspring thereof; and

causing female offspring, among offspring produced, to produce milk.

48. A process for producing a functional molecule according to Claim 47, wherein the first polynucleotide is introduced into the embryo so as to be operatively linked with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

49. A process for producing a functional molecule according to Claim 47, further comprising introducing, into the embryo,

a second polynucleotide encoding at least one of core 2β1,6-N-acetylglucosaminyl transferase-I (C2GnT-I) and core 1 elongation β-1,3-N-acetylglucosaminyl transferase (C1-β3GnT), and

a third polynucleotide encoding a polypeptide having at least one O-glycosylated region.

50. A process for producing a functional molecule according to Claim 47, wherein at least one of the second polynucleotide and third polynucleotide is introduced into the embryo so as to be operatively linked with at least one of the 5' regulatory sequence and 3' regulatory sequence of a gene relating to the mammary gland of a mammal.

51. A process for producing a functional molecule according to Claim 49, wherein the third polynucleotide is introduced into the embryo so as to be operatively linked with a nucleotide sequence encoding a signal sequence having effects of causing secretion of a polypeptide having at least one O-glycosylated region into the milk.

52. A process for producing a functional molecule according to Claim 47, further comprising milking after causing the female offspring to produce milk.

53. A process for producing a functional molecule according to Claim 47, further comprising isolating the recombinant functional molecule from the milk.

54. Milk obtained by a process for producing a functional molecule according to Claim 47.

55. A functional molecule obtained by a process for producing a functional molecule according to Claim 47.

56. A process for inhibiting bacterial growth, comprising:

contacting bacteria expressing cholesteryl-α-D-glucopyranoside (CGL) with a functional molecule having at least one α1,4-N-acetylglucosamine residue so as to suppress or inhibit at least one of growth of the bacteria and formation of cell walls of the bacteria.

57. A process for inhibiting bacterial growth according to Claim 56, wherein the functional molecule having an α1,4-N-acetylglucosamine residue can suppress or inhibit the activity of UDP-Glc:sterol glycosyltransferase.

58. A process for inhibiting bacterial growth according to Claim 56, wherein the bacteria are *Helicobacter* genus bacteria.

59. A process for inhibiting bacterial growth according to Claim 58, wherein the *Helicobacter* genus bacteria are *Helicobacter pylori*.

60. A process for inhibiting bacterial growth according to Claim 56, wherein the functional molecule having at least one α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

61. A process for treating gastric ulcer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue so as to alleviate signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* genus bacteria.

62. A process for treating gastric ulcer according to Claim 61, wherein the *Helicobacter* genus bacteria are *Helicobacter pylori*.

63. A process for treating gastric ulcer according to Claim 61, wherein the subject is a mammal.

64. A process for treating gastric ulcer according to Claim 61, wherein the mammal is one of mouse, rat, rabbit, horse, pig, sheep, goat and cow.

65. A process for treating gastric ulcer according to Claim 61, wherein the subject is human being.

66. A process for treating gastric ulcer according to Claim 61, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

67. A process for treating gastric ulcer according to Claim 61, wherein the administration is oral administration.

68. A process for treating gastric ulcer according to Claim 61, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

69. A process for treating gastric ulcer according to Claim 61, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

70. A process for treating gastric ulcer according to Claim 61, wherein the functional molecule is administered by using the milk according to Claim 54.

71. A process for preventing gastric ulcer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue so as to prevent signs or symptoms of gastric ulcer induced by the infection of a subject with *Helicobacter* genus bacteria.

72. A process for preventing gastric ulcer according to Claim 71, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

73. A process for preventing gastric ulcer according to Claim 71, wherein the administration is oral administration.

74. A process for preventing gastric ulcer according to Claim 71, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

75. A process for preventing gastric ulcer according to Claim 71, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

76. A process for treating gastric ulcer according to Claim 71, wherein the administration is performed using the milk according to Claim 54.

77. A process for treating gastric cancer, comprising administering a functional molecule having an α1,4-N-acetylglucosamine residue to alleviate signs or symptoms of gastric cancer induced by the infection of a subject with *Helicobacter* genus bacteria.

78. A process for treating gastric cancer according to Claim 77, wherein the functional molecule having an α1,4-N-acetylglucosamine residue is gland mucous cell-type mucin.

79. A process for treating gastric cancer according to Claim 77, wherein the administration is oral administration.

80. A process for treating gastric cancer according to Claim 77, wherein the functional molecule is administered by one of spraying and coating to the gastric mucous layer.

81. A process for treating gastric cancer according to Claim 77, wherein the functional molecule is administered by applying at least one of a film and a sheet, each containing the functional molecule, to the gastric mucous layer.

82. A process for treating gastric cancer according to Claim 77, wherein the administration is performed by using the milk according to Claim 54.

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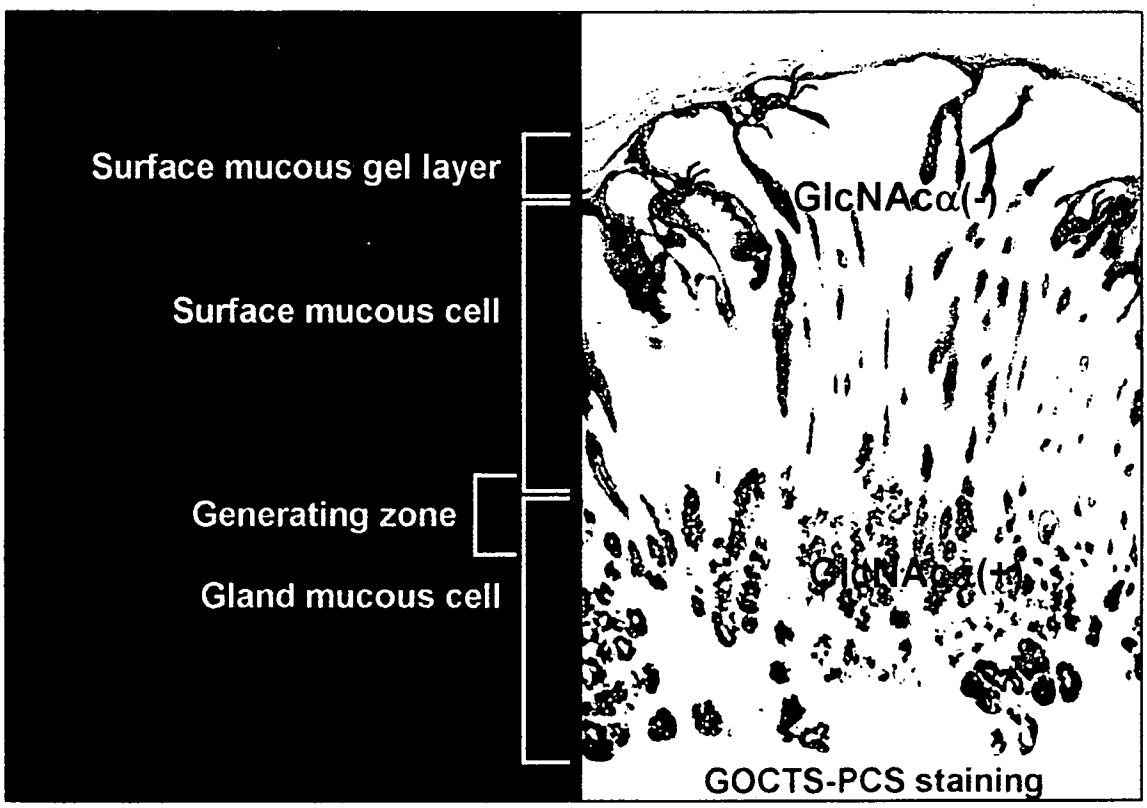
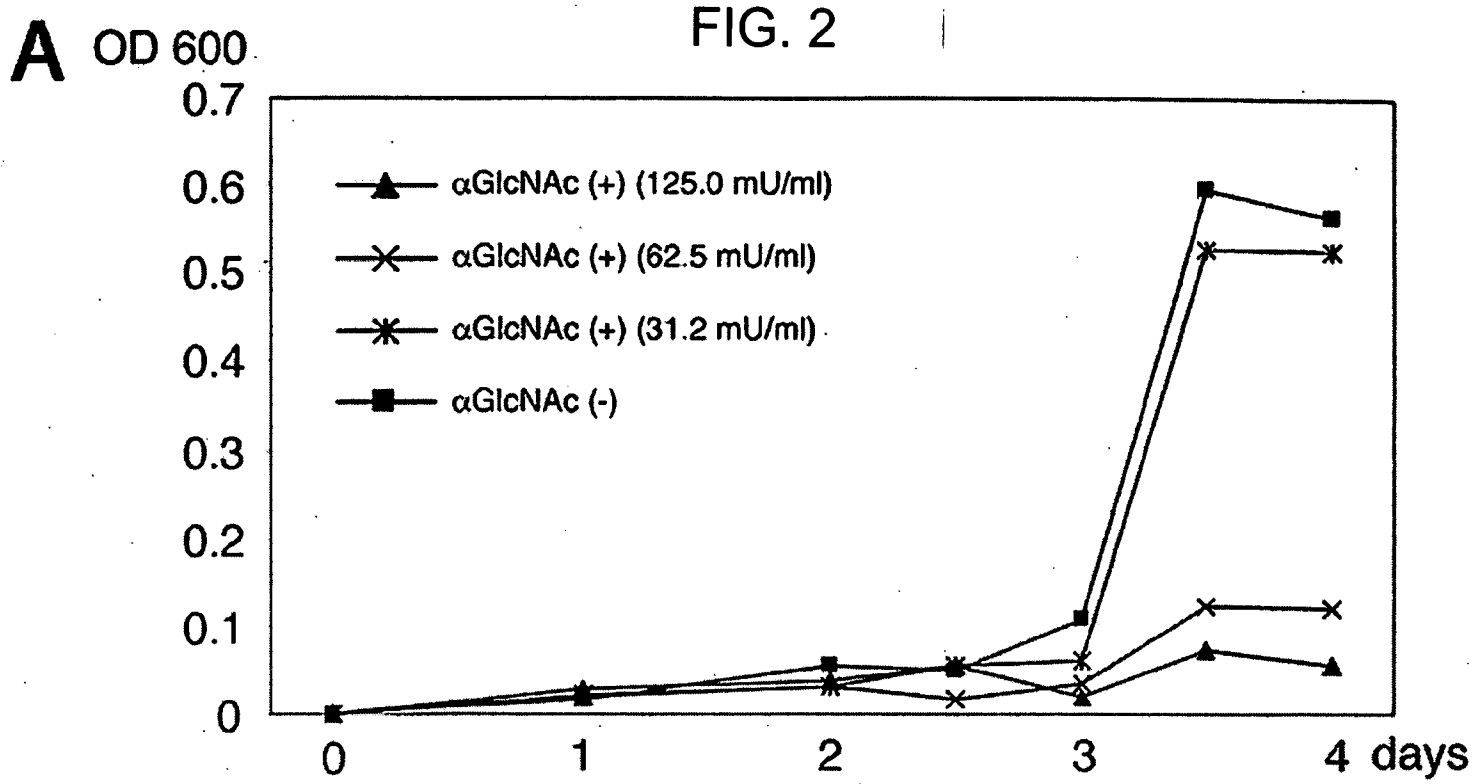
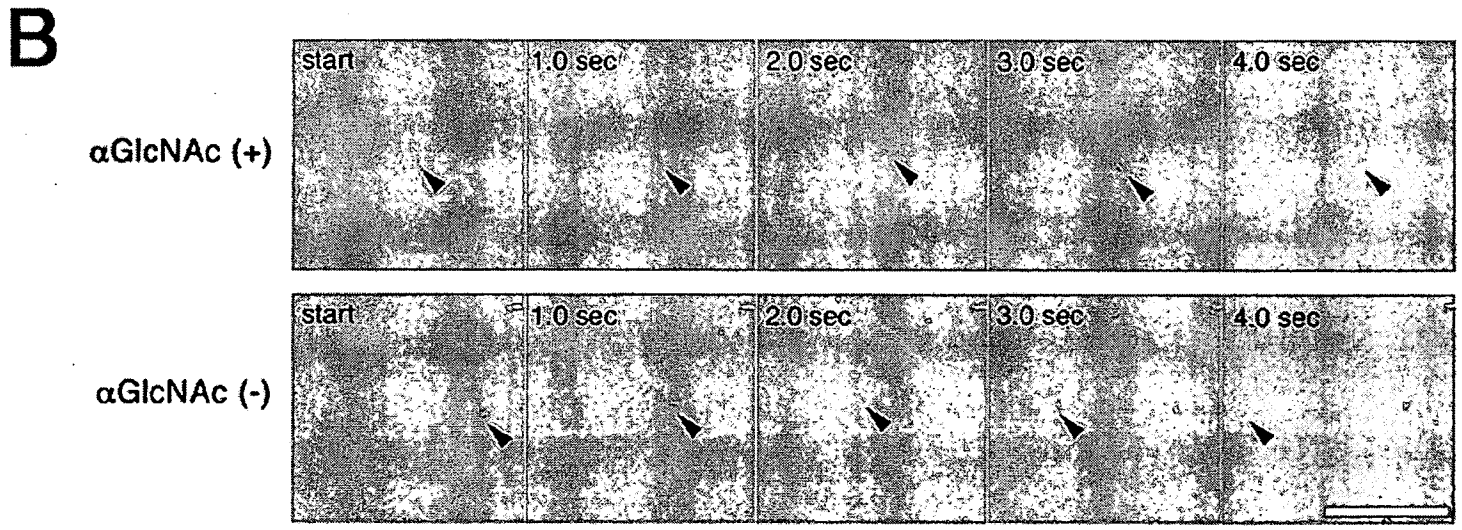
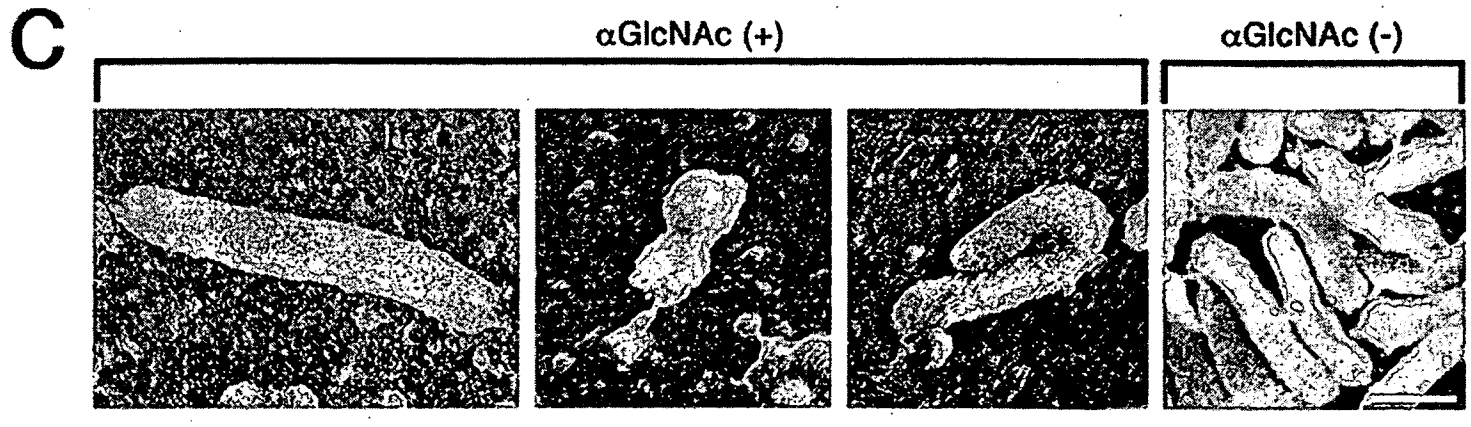

Surface mucous gel layer
Surface mucous cell
Generating zone
Gland mucous cell
GlcNAcα(-)
GlcNAcβ(+)
GOCTS-PCS staining

FIG. 1

FIG. 2


A
OD 600
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
αGlcNAc (+) (125.0 mU/ml)
αGlcNAc (+) (62.5 mU/ml)
αGlcNAc (+) (31.2 mU/ml)
αGlcNAc (-)
0
1
2
3
4 days


B
αGlcNAc (+)
αGlcNAc (-)
start
1.0 sec
2.0 sec
3.0 sec
4.0 sec


C
αGlcNAc (+)
αGlcNAc (-)

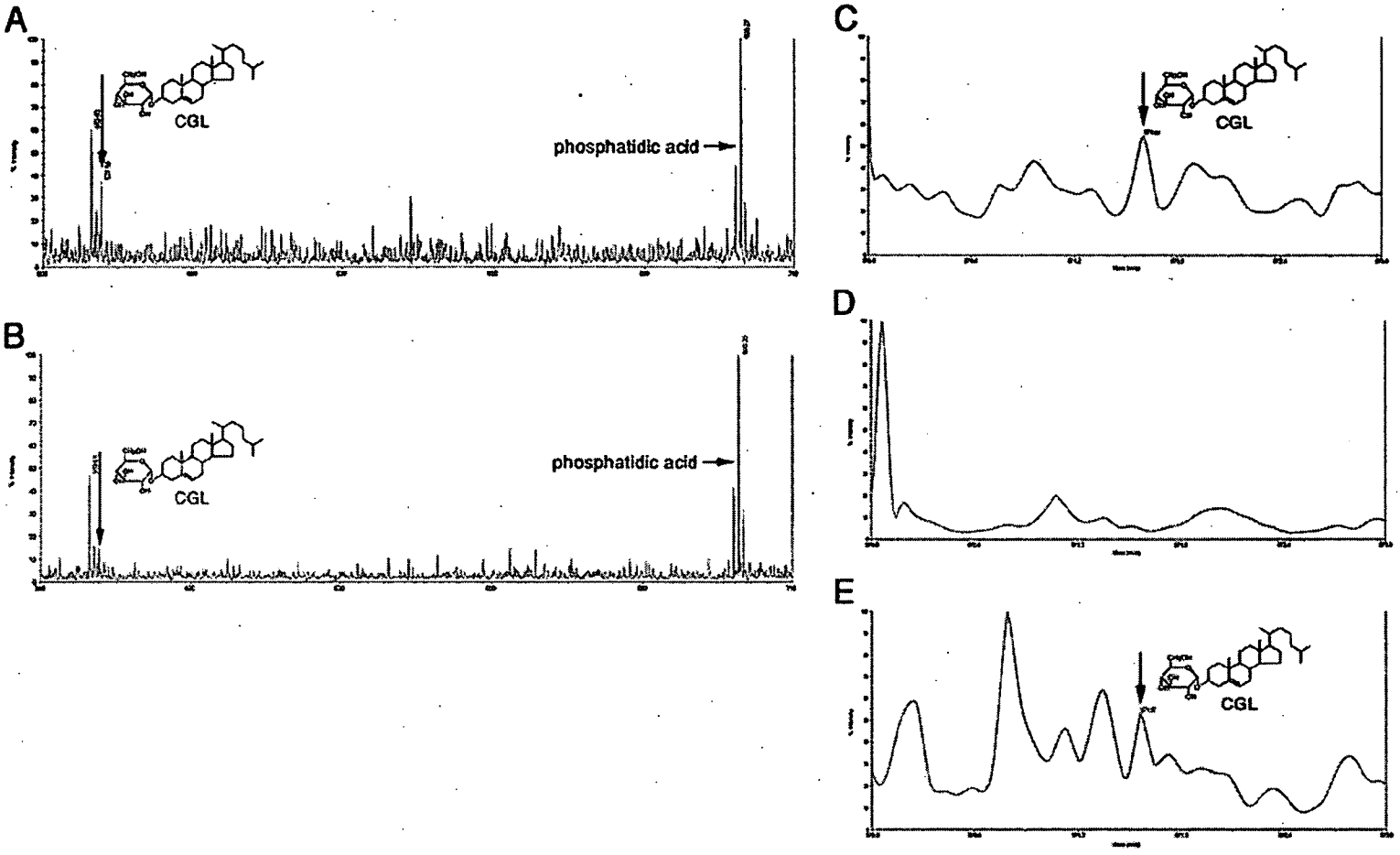


FIG. 3

CAG

CGL

CGP

1 2

FIG. 4

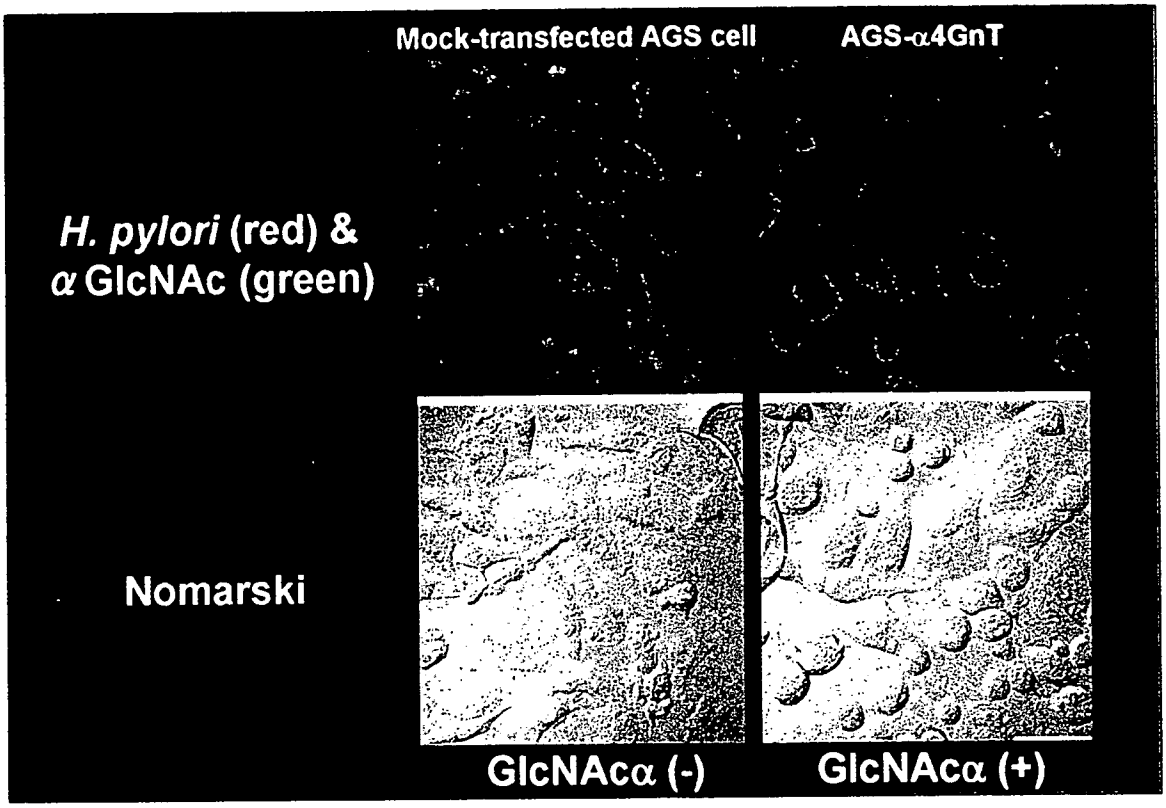

Mock-transfected AGS cell
AGS-α4GnT
H. pylori (red) &
α GlcNAc (green)
Nomarski
GlcNAcα (-)
GlcNAcα (+)

FIG. 5

MOLECULE, FUNCTIONAL MOLECULE AND PROCESS FOR MANUFACTURING THEREOF, COMPOSITION, PHARMACEUTICAL, FOOD, BEVERAGE, MILK, TRANSGENIC MAMMAL, PROCESS FOR INHIBITING GROWTH OF BACTERIA, PROCESS FOR TREATING AND PREVENTING GASTRIC ULCERS, AND METHOD FOR TREATING GASTRIC CANCER

ABSTRACT OF THE DISCLOSURE

Provided are a molecule, functional molecule, composition, pharmaceutical, food, beverage, and milk which are antibacterial, free from side effects and highly safe. Further provided are an efficient production process of the functional molecule; and a treating process for gastric cancer, a treating process for gastric ulcer and a preventing process for gastric ulcer, which are each antibacterial, free from side effects and highly safe. The molecule has an N-acetylglucosamine residue; the functional molecule has the molecule; and the composition, pharmaceutical, food, beverage and milk, each contain the functional molecule. The production process of the functional molecule uses a recombinant gene, and the treating and preventing processes for gastric ulcer and gastric cancer each include administration of the functional molecule. The N-acetylglucosamine residue is preferably at the terminal of the molecule through α-1,4-glycosidic bond, more preferably has a galactose residue adjacent thereto.